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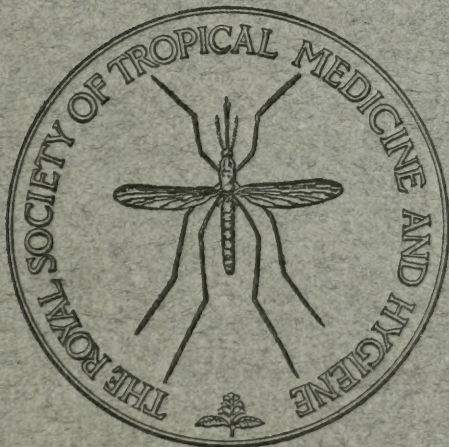
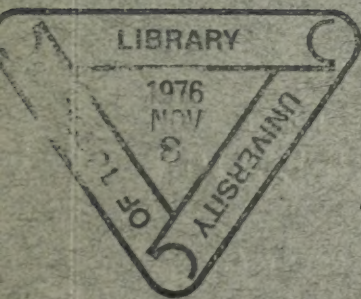
TRANSACTIONS

OF

THE ROYAL SOCIETY OF

TROPICAL MEDICINE

AND HYGIENE, *London.*



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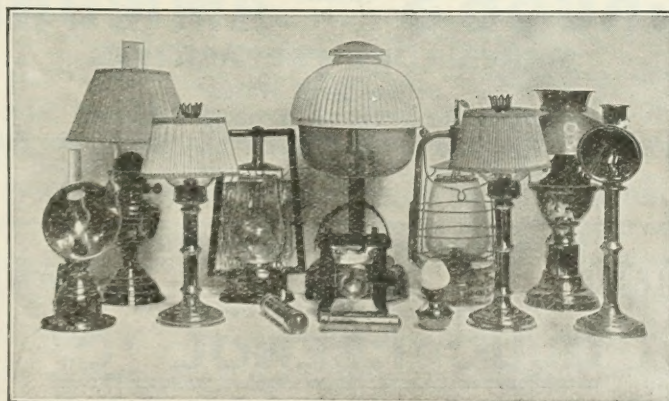
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W. 1.

TRANSACTIONS
OF THE
ROYAL SOCIETY OF TROPICAL MEDICINE
AND HYGIENE.

VOLUME XVI. No. 4.

Proceedings of a meeting of the Society held on Thursday, 19th October, 1922, at 8.15 p.m., at 11, Chandos Street, Cavendish Square, W. 1, preceded by a Demonstration of Spirochaetes of Rat-Bite Fever, by

Dr. R. ROW and Dr. T. JOEKES.

Sir JAMES CANTLIE, K.B.E., F.R.C.S. (*President*), in the Chair.

SOME CUTANEOUS MANIFESTATIONS IN RAT-BITE
SPIROCHÆTOSIS.

By R. ROW, O.B.E., M.D. (Lond.), D.Sc. (Lond.).

When Dr. WENYON did me the honour of requesting me to read a Paper before this learned Society, I hesitated in accepting the invitation, because I had not come to this country with any idea that I should have the honour of being asked to give an account of anything that I might have done; but the prospect of the joy of meeting my old friends in this Society, and also the prospect of rendering homage and paying my respects to the members of this Society, particularly as I know that most of you are my seniors in learning—though a few may be also my seniors in age—was so attractive that I accepted the invitation, and here I am before you.

I know my limitations, and the theme that I have chosen is not a very continuous one, so I content myself in venturing to give you a sort of mixed salad, the chief ingredients of which are rats, insects,

the flagellates and a vegetable, the meningococcus. I hope you will have the patience to listen to what little I have to tell you. Most of what I shall say has already been published, so I have little new matter to present to this Society.

The first portion of my remarks is in connection with rat-bite fever, a disease very common in India. Not only is it common now, but I think centuries ago it must have been common, too, because if we look into the writings of the old sages we find distinct descriptions of this disease. These great sages used to be famous for discerning the phenomena of disease, just as the ancient Grecian philosophers used to be. You will see on the right-hand side of the screen an original Sanscrit script, and on the other side, through the kindness of my friend, Dr. KHANOLKAR, I am able to show you the Roman script. There you have Shushrut, Wagabhatt and Yogaratnakar, the authors of three treatises which, when you come to examine and translate them, give descriptions which certainly strike you as very accurate records of observations, particularly when you remember that these writings can be dated back to about the third century after Christ. For our purpose I will take Wagabhatt, who worked seventeen centuries ago. I am not going to give the whole of his description of the disease, but in an account of the symptoms of a general irregular recurrent type of fever, a well-marked asthenia and anæmia, Wagabhatt refers to the cutaneous lesions produced by rat-bite, which he describes as follows:—"Burning in patches: nodular and urticarial eruption: petechial and even hæmorrhagic patches on the body: œdematous condition, discoloration and even ulceration of the nodules: lividity of the mucous membranes and hæmorrhages." The quotation I have given is from the Marathi translation read to me by some of my friends.

In India, unfortunately, we happen to belong to a race which is famous for quasi-humanitarian principles, and many pests are allowed to go almost wild. The rat and mouse, being rodents which breed very rapidly, have no chance of being destroyed as they would have been if they had been living in such practical countries as England or other Western lands. That is one of the reasons why I believe that the rat-bite disease, though described and recognised several centuries ago, has continued even to this day, and perhaps with greater virulence than in those early days. For the same reasons the plague

is always endemic in some districts. At one time, unfortunately, you had the plague in London, but the Great Fire destroyed it; but even if the fire had not come to your rescue you would have destroyed the rat and the flea, and with them the plague. But, as I say, our people are peculiar, and it is exceedingly difficult to get rid of these pests, which are responsible for the fact that rat-bite disease is common in our country.

Before I proceed to describe the actual disease, I might say that when the rat inflicts a wound on the patient it may be merely a scratch which passes unnoticed; or it may be in the nature of a very formidable cut involving deep structures, a very nasty bite such as one would expect from a rodent like the rat which has sharp incisors. A bite such as this would naturally be productive of inflammation with the consequent symptoms and signs, especially when we remember that during the bite of the rat not only the virus of the disease but various other organisms, such as the staphylococci and the streptococci and other septic organisms are introduced. Quite apart from any specific virus a very foul condition of the wound results. An enormous inflammatory swelling may develop, and with it we get all the accompanying symptoms of pyrexia. But in addition to that, in India especially, the ignorant classes have a very funny notion of the nature of "first-aid" which they give to a man bitten by a rat. They have certain kinds of dressings which they apply directly to the wound, and one of the chief ingredients of those dressings is an unadulterated mass of rat *fæces*. I suppose they look around and find *fæces* lying about and apply them straight off. You can well imagine that when a wound is thus further infected it is merely adding insult to injury, and you get severe inflammatory mischief produced, not only by the virus of the disease but also by the various septic organisms introduced by the "first-aid" of the ignorant classes. These septic organisms have been found by modern workers to be the streptococcus, the staphylococcus and the streptothrix, and I believe that these have been described as capable of producing rat-bite fever by men such as BLAKE and TIELSTON and RUTH TUNNICLIFF, the American workers. In this connection I take the opportunity of bringing to your notice the fact that I was disappointed when reading a recent and modern text-book on Tropical Medicine with reference to rat-bite fever, where the author did not seem to have read the recent works of other men, but only seems to give importance to this work of

BLAKE and TUNNICLIFF and TIELSTON; furthermore, he gives me the credit for having been one who ascribed the disease to a streptothrix. I take this opportunity of publicly disclaiming that honour. On the contrary, I said that rat-bite fever was purely and simply due to a spirochæte which I hope to describe, and not to the streptothrix or other septic microbes.

The lesion inflicted by the rat may be regarded as the primary sore, for it is here that the specific spirochæte is inoculated. It may be in the form of a scratch or ulcer, and may develop no further if treated properly with antiseptic dressings. If not so treated enormous inflammation may follow, leading to involvement of the whole limb with ankylosis of the joint. In one case it appeared as if gangrene would supervene, but this was averted. In other cases there is little of inflammatory reaction, the wound quickly healing and leaving a patch of glossy skin often devoid of pigment and slightly depressed.

Now the peculiarity of these local sores is that after a definite incubation period of seven to ten days—it may be shorter or longer—the site of the bite, which may be healing, becomes painful, and this is accompanied by severe fever, chills, and high temperature in the form of a relapsing fever. Each bout lasts three or four days, the temperature coming right down to subnormal. During one of these attacks appears the eruption which I propose to call the secondary eruption.

The secondary eruption is peculiar in this way: it varies in both quality and quantity. It may sometimes be a mere exanthematous rash, not easily made out in our Indian patients, partly on account of their being dark, and even in fair patients it may not be taken note of at all. The ordinary kind of rash which we get, for instance, is the rash which we saw in the case of the man whose photo I showed you first. The man had only five spots, which were noted fifteen days after the bite and five days after the first exacerbation at the seat of the bite. There were two spots on the left side of the chest below the clavicle, each perfectly circular in outline, quite flush with the skin and about one centimetre in diameter, deep purple in tint and petechial. There was another on the left side of the neck, somewhat like a split pea, with a round margin raised above the surface of the skin, almost reminding one of urticaria. There were two other spots at the back of the neck, very much like those at the side which showed signs of subcutaneous hæmorrhage.

The skin eruption in another case consisted of four thick cutaneous nodules, each being just like an almond, placed beneath the skin so that you could feel rather than see them, and all being painful and tender. They were situated on the inner side of the right thigh, and had ill-defined margins, and as the skin was in no way discoloured they could not be photographed.

Another case was that of a woman who had a very slight primary lesion which healed up when treated promptly. When the eruption and fever first attracted my attention, there was high temperature accompanied by spots, of which there were about six. Two of these, on the inner side of the thigh, were well marked, being black and almost hæmorrhagic in character, but quite flush with the skin. On the outside of the thigh there were four or five patches somewhat larger than the others and more like urticaria than anything else. The only way to diagnose the case as one of spirochætal fever is to obtain the history and discover spirochætes in the lesions.

Another case, which first gave me my experimental virus, is important from the point of view of the extensive nature of the lesions. The eruption appeared in the third attack of fever and was papular: it commenced on the face, and then extended to the neck and trunk and, lastly, to the extremities, and at each paroxysm of the fever the older papules became darker and harder, and tended to peel off on the surface. I saw the patient on account of the high temperature—it was 105° at the time—his face was flushed and there was a shine over all the nodules, raising a suspicion of its being nodular leprosy. I had never seen the boy before and the history we got was somewhat vague. I had the opportunity of examining a small quantity of fluid from one of the papules and thereby found out the actual cause of the disease.

The blood squeezed out of the lesions of such patients gives no particular indication of any disease. Considering the extent of the inflammation one would have expected to find a little leucocytosis, but this was absent in my cases.

The blood serum was tested for WASSERMAN reaction with negative result. I could never get anything in the shape of cultures, even from the first case, which was full of parasites. One of the ways in which I have always succeeded in trapping the spirochæte is by taking blood from the zone of the primary sore. It may be very difficult to get

a person having the secondary eruption, but the primary sore is always easy to obtain. The inflammatory ring round the primary sore is punctured, and the blood-stained fluid thus obtained is injected into mice. It may be impossible to discover spirochætes in the fluid from the sore on account of the quantity of blood corpuscles present, but the organisms appear in the blood of the mice. An important point is that the blood of the patient when in high temperature has been found by me to be absolutely non-infective to mice.

I am reminded, by that statement, of what happened when I gave infected mouse's blood into a monkey which developed a temperature. I gave a small quantity of his blood into a guinea-pig, and the guinea-pig's blood was found full of spirochætes about ten days later. It is sometimes necessary to pass in to a monkey and then into a guinea-pig to detect the spirochæte.

The spirochæte may be found in the serum that is squeezed out if you are lucky enough to get less of blood and more of serum. It is a very fine spirochæte, showing generally one and a half curves and sometimes two, but very rarely three, and when there are more than three, it is generally in a division form. It is interesting to compare them with the spirochætes which have been exhibited here by Dr. JOEKES. They contrast with the spirochætes I have shown under the last microscopes on the table. Mine are very fine and without flagella, while those of Dr. JOEKES are thick with three or four turns and provided with flagella. I do not find any difference, whether they come from the mouse or human being, in their morphology, their staining reaction, or want of flagella. I always find them the same, whether the mouse is in an early condition of infection, or even after six weeks or six months after infection. The mouse does not seem to react quickly to the infection, although he suffers ultimately, for at the end of six months he is emaciated, and often suffering from loss of hair.

I might point out that the organs of experimental animals do not contain any more spirochætes than would be contained in the blood supplying the organs. So also in man. It has been suggested by some Japanese workers that the kidney was the most infected organ, and I thought perhaps it would be worth while to examine the sections and the serums from various organs, and from my observations I think I am safe in saying that spirochætes are no more numerous than would be accounted for by the blood found in the organs.

When the spirochæte is stained by the silver nitrate method you get a thick rod with two curves, the spirals being obscured, but it can be recognised to be a spirochæte. The silver deposit makes it appear thicker, but I have obtained no indication of terminal flagella. The photographs which I am showing were taken by Dr. COLES, of Bournemouth, from specimens I sent him. If you compare the blood corpuscles you will see the size of the spirochæte is not more than one quarter the diameter of the red corpuscles. Some, which appear larger, look like one individual, but, as a matter of fact, if they are examined it will be found that two are apposed end to end.

I should now like to say a word or two on recent work in connection with the disease done by other people. Curiously enough, Japan seems to be very fertile in this disease, perhaps on account of the Japanese being Buddhists. They also, as in India, do not like to kill animals, and probably for that reason the disease is endemic in Japan also. It is called there by a particular name. HATA, when he studied the disease in Japan in 1912, thought that it might be a spirochætal infection and reported the cure of eight cases of rat-bite disease with salvarsan. But it was not till 1916 that the spirochætal nature of the disease was demonstrated by four Japanese workers—FUTAKI, TAKAKI, TANIGUCHI and OSUMI—who described the parasite in their cases of rat-bite fever. They said it was a little longer than *Spirochæta pallida*, something between *Sp. duttoni* and *Sp. obermeieri*. But later they made another communication in which they drew a distinction between the shorter forms and the longer ones, according as the spirochætes were found in the peripheral blood of the human rat-bite cases or in the lymphatic glands. The one found in the latter situation was said to measure from 2μ to 3μ , and the one from the peripheral blood 6μ to 8μ . They found also terminal flagella.

Later, in a communication published in the *Journal of Experimental Medicine* of America, we find other men also giving descriptions of the spirochætes found. There seems to be a great deal of difference of opinion with regard to the results obtained by the Japanese workers. For instance, the spirochætes studied by OHTAVARA and TAMURA, though closely resembling the short form of FUTAKI, are described by the authors as being different from those of FUTAKI, not only in morphology and general distribution, but also in their behaviour in guinea-pigs, to

whom the spirochæte is said to be not only pathogenic but virulently fatal. These spirochætes are of interest, as they have some bearing on the human rat-bite spirochætosis in its relation to experimental rat-bite spirochætosis, although this was induced by a particular class of biting rats.

The other workers, KATAGAWA and MUKOYAMA, in their description seem to lay special importance on the two distinct forms, the long and the short type, and they claim that the former is quite different from that of FUTAKI while the latter is identical with it. In any case they seem to differ greatly among themselves.

Considering all these differences in the spirochætes described by the Japanese observers and also of the spirochætes I described lately, I thought it would be interesting to see if the Bombay spirochæte is identical with that from Japan or different from it, and also if more than one species of spirochæte is responsible for this disease. I suspected that the spirochæte which I described might be a different species, though not of a different order altogether, because I found distinct differences. And that is the reason why I ventured to call it by the name of *Sp. petit*, partly because it was a very small spirochæte, but chiefly because the work I did was done in the laboratory going by the name of the Petit Laboratory, founded by the brother of Mr. B. D. PETIT, whose picture I saw in your Tropical School.

Before I conclude this part of my subject I should like to show you the pictures of FUTAKI's spirochæte.

In concluding the remarks I have to make on the spirochæte I might just summarise the distinctive features I found from my own study of the Bombay specimen. I came to the conclusion that the spirochætes derived from the human lesion are identical with those recovered from the peripheral blood of the white mouse or guinea-pig infected with the human material. Secondly, that the Bombay spirochæte is smaller than even the small variety of FUTAKI and the small type of KATAGAWA and MUKOYAMA, and is practically of uniform size. Thirdly, that the broad distinction made by FUTAKI into the long and short forms according to the situations from which the virus is derived—the long form from lymphatic nodules and short ones from peripheral blood—does not hold good in Bombay, where all that are found are short, and measure from 1.5μ to 2μ in length, any slightly longer forms detected being distinctly division forms

of the same. The spirochætes are found only in the cutaneous lesions and not in the peripheral blood of the Bombay cases. I am not quite certain, but it seems to me that my spirochæte resembles the one which you have seen here in London, but I hope there may be an opportunity of comparing it with the Bombay strain.

I may add that no lymphadenitis has been noticed in the cases under observation, and that I have not been able to satisfy myself as to the presence of terminal flagella, although the ends of the Bombay spirochæte are pointed. Further, the behaviour of the Bombay spirochæte in experimental animals is different from that of the Japanese type. It is not fatally virulent to guinea-pigs and rats.

I should like now to show one or two photographs of the cultures of the relapsing fever spirochæte, because these cultures have been very difficult to make in Bombay. Dr. WENYON informed me that he also found it difficult to get the subcultures. Unfortunately, I have not succeeded beyond the third generation. I would like to show you what I did, in the hope of getting information from you or some advice as to how I might proceed.

Here is the spirochæte as you find it in relapsing fever. This is the sort of culture I succeeded in getting by simply taking the infected blood and putting it in small tubes with two per cent. glucose. This was the first generation. This is the same thing, and I hoped it would continue, but to my disgust after the second or third week I got poorer and poorer subcultures. The spirochætes all became smaller and thinner and more divided, and ultimately there was nothing left but débris.

SOME PROBLEMS IN CONNECTION WITH THE STUDY OF THE ETIOLOGY OF LEISHMANIASIS.

Our knowledge of the etiology of leishmaniasis is anything but satisfactory. Some people have been working ever since the time when the *Leishmania* parasite was found to grow into a flagellate. All the attention of workers has been directed to finding a transmitting insect—an insect in which natural flagellates could be found or one which could be infected by making it bite certain infected animals containing the virus, and in which the flagellate form would develop in the intestinal canal. To a certain extent, it is pardonable that so large an amount

of work has been done along this line, because we have the analogy of the tsetse fly and sleeping sickness. With some the belief has been almost a fixed idea. In spite of there being no convincing proofs or single positive experiment of insect infection, they still hold to the belief that certain classes of insects are responsible for the disease, because an enormous number of flagellates may appear in the intestine when such insects are fed on material containing the original virus of the disease. Of course, to a certain extent, I may say that the discovery of the flagellation of this parasite has been more a curse than a blessing, because much of our energy has been dissipated in looking at these beautiful flagellates, their sinuous movements, their beautiful colouring when stained, and the beautiful pictures they produce. I suppose that arrests our attention to such an extent as to cause us to think that so long as we can get flagellates in biting insects we are on the right track of finding the etiological factor and the carrier. So the mosquito, the flea, the bug—I believe that is the chief one—and the sand-fly, have been one after another condemned, and by some held to be the real carriers of the disease. When one remembers what happens to the flagellate stage of this parasite when it is first of all subjected to the ordinary process of serum action outside the body, when a mass of culture is mixed up with serum and examined under the microscope, one finds that the serum has got such a solvent action on the parasite that in a few minutes—perhaps at the end of half-an-hour—the whole flagellate breaks up and you see nothing but débris. So that when these treated flagellates are cultured it is almost impossible to get a subculture from this material. Some other workers, chief amongst them being CORNWALL, who is working in Coonoor, have extended this observation by submitting these flagellates to emulsions of liver, spleen and bone-marrow cells, and they have found that in about twenty minutes they could not only kill them but could not even recognise them under the microscope. So with such a delicate organism as the flagellate it is no wonder that we can never succeed in getting an infection. What I mean is that if you get culture containing nothing but flagellate in hæmoglobin medium, N.N.N. medium, and give even massive doses to very susceptible animals such as the mouse, you will certainly not get infection. But by giving old cultures, containing post-flagellates (because they are altered into what we may call post-flagellates), especially if we administer to the animal repeated injections,

we can produce disease ; it is an intensive method of infection. In this way I have been able to produce a generalised infection with oriental sore virus. That, of course, is a thing which has been published, and of which I gave an account in one of the journals in 1912.

Therefore, to sum up, in order to get a real infection we must have the resisting or resistant form of the parasite. I think we can say in comparative terms that the body which you find in the lesions, such as those of oriental sore and the O body (the round form found in old cultures), may be considered more resistant than the flagellate. In all insects, up to now' attention has been directed towards flagellates, whether the flagellate of the gut or elsewhere, and wherever actual flagellates are not found it is assumed that the insect is of no use. But in cultures this aflagellate condition can be brought about by using solid media ; in fluid media there is an enormous number of flagellates, though, of course, occasionally O bodies are found, and these have been described by all workers on the subject. But I have hit upon a plan of testing the growth of the flagellate on a solid medium.

Cultures on solid media were made by MANCEAUX and NICHOL as long ago as 1911, but in their description I cannot find anything beyond the statement that they found O body forms in their cultures. That was not quite enough, because O body forms are also found in fluid media cultures. So I thought of studying the cultures on the surface of N.N.N. medium. If the tubes are slanted a few of the flagellates are stranded on the dry agar, and these multiply and grow in a sort of quasi-amphibious form, and give rise to colonies which at the end of eight days can be watched with the naked eye. If this film is scraped off and then put in saline it will be found that there occur not only flagellate forms in very vigorous condition, but also O bodies, the development of which from the flagellate can be traced week by week.

There is a certain class of flagellates which can be found in plants, and I think that sufficient attention has not been paid to them. I do not say that the plant flagellate is one of the things which might have any relationship with the kala-azar, but we have in India such a rich flora and such a rich fauna of insects that it is just possible—only tentatively I say it—that some of the insects might carry these flagellates and develop them in such a way as to produce these particular cryptic forms which ultimately give rise to the disease. I propose now to show you, by means of the epidioscope, the flagellates in these plants,

and then proceed to summarise the various changes undergone by the flagellates on solid media. In the first instance, there is the multiplication of the flagellates into all shapes and sizes, the main features of which are a long and active flagellum, vigorous motility of the parasite and uniform staining characters and well-marked differentiation of the nucleus. This active multiplication goes on for one or two weeks.

There is a differentiation between the inner and the outer part of the body; the outer part being pale. The second phase shows the flagellum withdrawn. The portion of the body which is inside can be distinctly made out as a torpedo body, outside which is the shell, and, lastly, the parasite assumes the form of the O body. The rudiment of the flagellum is withdrawn, the parasite gets condensed, and the O body is produced. Finally, the outside shell-like membrane is cast off and absorbed or destroyed.

From what I have described here it may be permissible for me to suggest that in trying to search for the carrier by the study of intestinal contents of insects, we are brought face to face with enormous numbers of these flagellates of different shapes and sizes, so that when we miss these occult forms we are missing something which may be really an infective agent. Therefore, for the future we should, I think, search for these forms where at present they do not apparently seem to exist.

If we consider the various insects which are blood-feeders, we find in the rectal contents some bodies which may be like the O bodies I have described, or some other occult forms that may lead to some positive results. I want to point out this fact, that in the rectal content of insects there is much we have to work out. I should personally feel obliged for any suggestions that might come from you.

With regard to phlebotomus, we all know the views suggested by SERGEANT and his brother working in Tunis. They suggested that the oriental sore—there it is called by a different name—is propagated by the phlebotomus, and they have suggested that the phlebotomus takes up the virus from the Grekko. I have examined about a hundred lizards from different places where oriental sore is prevalent, and I am sorry to say not one of them was found to be infected. I myself think, if I may judge by the number of flagellates they contain, that the plant may act as a greater reservoir than animals, and as we have so many plants and insects we have a great field to work in, and I hope in future we may come to some

definite decision about these troublesome diseases, particularly kala-azar.

Before I close this part of the programme I might show you one or two cases of leishmaniasis which might interest you. Dr. BALFOUR published an account of certain observations he made in Khartoum. He described a non-ulcerating form of leishmaniasis which resembled the lesions in a case I now have in mind. I saw the case at the Lady Hardinge Hospital where I was working, and the man showed me peculiar nodules which reminded me of Dr. BALFOUR's case. I showed this case to many of the Medical Officers in Bombay and asked for their diagnosis, but they did not seem to recognise it. I was surprised to find it was a case of non-ulcerating leishmaniasis. Although these non-ulcerating forms are not common, we do get them in some localities, and they are very interesting in that they are not quite like the Keloid tumours described by Dr. BALFOUR, but more like *molluscum fibrosum*.

In connection with the treatment of leishmaniasis, I had the opportunity of studying the effects of a vaccine of *Leishmania flagellates* in the cases of oriental sore, and, though I have not published recent results, I can state with confidence, from the work that was done in the War Hospital in Bombay, where we used to get a large number of cases from Baghdad, that the use of 1 c.c. or 2 c.c. of glycerinated vaccine of young flagellates has yielded very good results in the main, while there were instances in which the results were quite satisfactory.

A CASE FOR DIAGNOSIS.

The third part of my Paper will not take long, so that I hope you will give me a few minutes more. I will just read particulars of the case and hope you will be able to help me in the diagnosis.

The patient, a child of ten years, Mohammedan, female, apparently in good health, went to a fair in connection with the celebration of an annual feast in a mosque located on an island a few hundred yards from the shore, and returned home in very good spirits. A few hours after reaching home she complained of shivering and fever, and was put to bed. The next morning she was seen by a doctor, who found her in a serious condition, with a temperature of 105°, very feeble pulse, and inability to retain food or medicine, and showing a peculiar rash all over the body—a rash which resembled irregular petechiæ, not suggestive of any exanthematous rash generally seen in Bombay. The examination

of the chest and abdomen revealed no disease. There were no nervous symptoms indicative of any cerebro-spinal mischief. All that could be observed was the hyperpyrexia, the rash, which resembled that of typhus exanthemata, and a very feeble, quick pulse. When I saw the child in the evening I could find nothing beyond these phenomena, except that the pulse was not felt at the wrist. The most remarkable feature was the perfectly clear way in which the child could answer all questions put to her, even when in *articulo mortis*. All I could do was to get, with very great difficulty, a small quantity of peripheral blood, enough for a smear on the agar surface and on a glass slide. The agar smear was taken to the laboratory, and a subculture was made immediately in an N.N.N. tube and the slides stained and examined. The smear revealed the features seen in the lantern slide, and the culture gave results of a meningococcus, and was very virulent to white mice. It was not possible to confirm the identity of the culture by serological methods. Although I have kept a close watch for similar cases in the neighbourhood, and wherever I could, I have not been able to see the like again.

I have no more to say except to thank you for the patience with which you have heard me. I feel particularly delighted to meet you, all my seniors, and to pay my highest regard and respects to you. I feel particularly touched by the presence here of Professor SIDNEY MARTIN. I take the opportunity of making this personal reference, because it was sitting at his feet twenty-five years ago that I first drank the draughts from the fountain of research and whose invigorating tonic effects have not yet disappeared. I hope they will continue for some time. With these few remarks I thank you all very much for your patience.

DISCUSSION.

Dr. A. POWELL: I congratulate the Society on having heard from his own lips an account of the valuable researches of my old friend, Dr. Row.

I can thoroughly sympathise with him for the way in which he has been treated by our modern text-books. BYAM and ARCHIBALD'S book treats rat-bite fever as a rare disease—"eighty cases altogether have been reported . . . the majority, about one-third of these, from Japan." I have personally seen at least forty cases in Bombay since 1901. Many

of these, before Dr. Row discovered the parasite, were only diagnosed clinically. Between 1915 and 1919 there were thirteen cases in the Bombay City Police of 3,000 men, approximately one per thousand per annum. In Bombay it therefore cannot be called a rare disease. In these thirteen cases I found Row's spirochætes in eight. I sent many of the cases in which I failed to find the parasite to Dr. Row and he usually succeeded in finding it.

C. C. BASS, *apud* BYAM and ARCHIBALD says :—" In a case recorded by Row a very short streptothrix was isolated—the cause of the disease. It is possible that this is the same organism *Streptothrix muris ratti*, described by SCHOTTMÜLLER and BLAKE." I need hardly say Dr. Row never said such nonsense.

MANSON-BAHR's text-book does not mention Row's parasite nor does it mention India in the geographical distribution of rat-bite fever.

My observations completely agree with Dr. Row's description of the Bombay parasite. In all my cases and in all I have seen of Dr. Row's, Dr. BANA's and other cases, the spirochæte was short, about 3.5μ long, with an average of two and a half spirals.

I have never seen a flagellum, though in all cases slides were stained with Giemsa, and in two with iron-hæmatein. I have never seen the long spirochæte described by the Japanese nor any like those shown by Dr. JOEKES to-night.

My observation of the skin eruption differs somewhat from that of Dr. Row. As the wound caused by the teeth of the rat is almost always septic, a mixed infection results. You may have a large septic, even a sloughing wound as a primary sore, or it may be a mere scratch which becomes indurated and painful, not only at the onset of the fever, but also at some of the later relapses. By far the most characteristic lesion was a secondary eruption of dusky blotches about the size of a shilling or a sixpence, sometimes larger, sometimes smaller. These blotches are of a livid or dusky purple colour, slightly raised above the surface. I have never seen any that I could call nodular; few have their margins raised steeply enough to be called urticarial.

A very characteristic appearance is a fine roughness or stippling in the centre of the blotches, looking at first sight like a number of minute, closely aggregated sudamina. With the help of a lens these dots are seen to be papillary and not vesicular. When the rash is fully developed, pressure does not cause the colour to disappear completely.

These blotches may be numerous, but often there are only four or five on the whole body. In two or three cases I have failed to find any secondary rash. As the eruption comes and goes with the febrile relapse it is possible patches escaped my observation. Patients always complain of pain in the primary sore, and often of pain and burning in the secondary patches.

Dr. T. JOEKES: After I had had the good luck of seeing, within the space of twelve months, three cases of rat-bite fever contracted in this country, my interest in this disease was aroused. Through the kindness of the Wellcome Bureau for Scientific Research I have been able to investigate some points of special interest in connection with this condition. So far I have been able to isolate nine different strains of the *Spirochaeta morsis muris* from wild rats caught in London. I am not going to worry you with all kinds of details which would not interest you, but there is one point I want to draw your attention to, which may prove to be of rather great importance. In his paper on rat-bite fever, and again to-night, Dr. Row told us that he has never been able to see flagella in his spirochætes, neither in a dark back field nor in stained films. Now we have found in all our strains quite distinct flagella, as you have seen in the fresh dark background films and in the stained films I put out to-night. As the technique of demonstrating the flagella is so very simple—for the stained film one has to make thin films and stain in the ordinary way with Leishman—one wonders whether perhaps the spirochætes found here in England and those found by Dr. Row in Bombay are different species. The spirochætes in Dr. Row's films are, on the whole, certainly smaller than those in my films; but it would be important to know at which stage of infection Dr. Row's films were made, as we found that very often at an early stage the spirochætes are very small and slender, to become bigger and longer during further development. The young stages we found to possess terminal flagella only, whereas later on they show lateral ones as well, these latter being located more or less in the middle of the spirochæte, at the place where the division is going to take place, after which division we again have two small spirochætes with terminal flagella.

Dr. ANDREW BALFOUR: I am sure the Fellows of the Society much appreciate the opportunity that has been afforded them of hearing Dr. Row's paper. Dr. Row's name may not be in the text-books, but

some of us have seen him at his work in Bombay and appreciate how keen and earnest he is in that work.

Of rat-bite fever I know very little. I have followed with some interest what Dr. JOEKES has been doing, and I happen to have a very interesting painted picture of the rash of rat-bite fever in a Spanish case. The appearance is erythematous, such as is usually described. There is none of that nodular aspect we have seen in the lantern slides.

The question of leishmaniasis is of course a very difficult one. We seem to be at a deadlock as regards the method of transmission of *Leishmania donovani*. No doubt many of us have read a paper by Lieut.-Col. MACKIE, of the Indian Medical Service, in which he reviews the whole situation. I cannot say anything to throw light on the vexed problem, but I think the point of view put forward by Dr. Row that it would be of great interest to examine the dejecta of the various insects which have so far been incriminated without, however, any definite proof, is a helpful one. I notice that one of Dr. Row's compatriots, Dr. AWATI, has been carrying out a survey in Assam, and has been examining all the native houses there, both in infected and uninfected areas, collecting in them during the season when kala-azar is prevalent and also when it is not so prevalent, the various insects which lodge in these dwellings. He has collected a very considerable number. One point of interest I noted was that the only species of insect which was present in the infected area but not in the uninfected area was a *Conorhinus*. After what Dr. Row has said, I think it would be of interest if Dr. AWATI was to go further and, in addition to collecting these insects, examine their dejecta.

I was interested in seeing those photographs of the non-ulcerated type of oriental sore. As Dr. Row says, they are not quite similar to those which I described in the Sudan long ago with Captain DOUGLAS THOMPSON of the R.A.M.C. These were more of the Keloid type. But there is a very considerable general resemblance. It is clear that there are many varieties of oriental sore and also probably a good many varieties of this non-ulcerating form. One of the most recent cases recorded is one by BRAHMACHARI, in which the whole body was studded with closed lesions of this kind, but this remarkable variety does not seem to be altogether new, because CHRISTOPHERS, of the Indian Medical Service, described something similar a good many years ago.

Lastly, there is the curious case for diagnosis which Dr. Row has

submitted to us. I am afraid nobody can do anything but guess. In the first instance one naturally thinks of some peculiar form of cerebro-spinal meningitis. I fancy that is really Dr. Row's diagnosis. At the same time it should be noted that the child had been at a fair. There is therefore the possibility of food-poisoning to be considered. We know that in food-poisoning you sometimes get remarkable rashes, and occasionally sudden death without very marked symptoms. As a rule, however, there is intestinal trouble and no marked change in the temperature. Was the possibility of food-poisoning excluded? On the whole, I should say the case was almost certainly one of fulminant cerebro-spinal fever.

Dr. H. H. SCOTT: On the first two subjects I have nothing to say, but on the third I have. I had one case which is strongly analogous to this case Dr. Row has described and which was reported in 1916. The facts of that were, briefly, as follows:—The man, who was with one of the Canadian contingents, was absolutely well until 7 o'clock one evening—15th December, 1916—when he suddenly fell ill and had a shivering fit, the temperature rising to 104° . During the night there was nothing particular at all and he felt fairly well; temperature gradually dropped. Next day it was 102° , and he was taken into hospital at 4 o'clock, when I saw him for the first time. There were a few petechial spots; he had a certain amount of pain in the legs and there was Kernig's sign present. He was sent to an Isolation Hospital for observation, and he got there between 7 and 8 p.m., absolutely rational, no headache, no vomiting, no convulsions, no delirium, nothing but this temperature, the rash and the leg symptoms; he was absolutely clear mentally. He was perfectly alert until 8 o'clock, but died at ten minutes past—only twenty-five hours after the original onset. I obtained pure culture of the meningococcus from the spinal fluid and also from the blood stream itself. This case seems closely analogous to that brought forward by Dr. Row, both as to the rash and mentality up to the time of death. It was reported in the *R.A.M.C. Journal* at the time.

Lieut.-Colonel MARRIAN PERRY: I agree with the last speaker regarding the case Dr. Row has brought forward for diagnosis. There is little doubt that, if the facility for serological identification of the organism isolated was available, he would have found it to have been the meningococcus.

I have had experience of three fatal cases of very similar nature,

arising in France, which were proved by blood culture to be meningococcal septicæmias. The duration of illness corresponded closely to this case reported from India.

Dr. P. H. MANSON-BAHR: I had in 1916 a curious case very analogous to Dr. Row's, which I think bears a resemblance to a pneumococcal septicæmia. A man was brought in extraordinarily ill from the barracks in Cairo, and he died exactly four hours after admission to hospital. He had a rash which was thought to be typhus, and when I was searching through the blood film I came across leucocytes containing diplococci, which I took to be pneumococci. The post-mortem examination bore out the diagnosis of an acute pneumococcal septicæmia. So it shows that even in pneumococcal septicæmia you can get the particular rash and so forth that has been described in these acute meningococcal cases. I have no doubt they can, under certain circumstances, behave very much in the same way.

Dr. R. Row: I can only again express my gratitude for the kindness with which you have received what I had to tell you. It has taken up much of your time, but, anyhow, it adds to the gratitude I feel towards you.

With regard to the remarks made by Dr. JOEKES, I feel inclined to think that the technique which I have adopted in staining my specimens does not differ in any way from the technique which he employs. Besides that, the specimens sent to Dr. COLES, of Bournemouth, have been stained by him in his own way; and he found also, as I have found, that the spirochæte seems to be much finer and much smaller. It does not seem to increase in size as time goes on, and it is of the same morphology both in the beginning as in the end. It is just possible that in the early forms the curves may be only one-half to two, and, later on, two or two and a half curves. But, at any rate, the longer forms are distinctly divisional forms and devoid of flagella. That is one point I want to emphasise.

The other is that, from the specimens I see here, even the smallest seem to be a distinct species; they appear to be much fatter, and to be like a spindle pointed at both ends, and also with closer curves. At any rate, it strikes me as possible that the spirochæte that I described as the Bombay one seems to be quite unlike the spirochæte that Dr. JOEKES has identified, and has been kind enough to show. It has given me an

opportunity of comparing it with the spirochæte that I have described, and it strikes me, from the short time I have been able to devote to it this evening, that it resembles more the spirochæte of the Japanese workers.

As for the culture, I am in the same position as Dr. JOEKES. I have been trying to culture the spirochæte ever since it was isolated, but, unfortunately, I have not made any progress. I hope, as I said in the course of my remarks, that by learning from you gentlemen the technique of hydrogen ion concentration I may be led to the discovery of a medium which will prove successful. The spirochæte of rat-bite fever seems to me more delicate than the spirochæte of relapsing fever, and much more delicate than the spirochæte of icterohæmorrhagic jaundice.

With regard to the kind remarks made about the case for diagnosis, Dr. ANDREW BALFOUR spoke of the rash. It was universal. It is exceedingly interesting and instructive to me to learn from our friends here that they also saw four cases of fulminating meningococcal disease. I am very glad to see that the diagnosis has been pretty nearly confirmed. To my mind it was a case which appeared to be very mysterious and very doubtful, except for the fact that I saw an organism very much like meningococcus. I could not, however, come to any conclusion; all I could say was that it was remarkable that there was only the one isolated case. It is possible that the child may have eaten some injurious substance. The case was so very rapid that it appeared more like poisoning than anything else. The cause of the illness was obvious when the microscopic examination was made. I again thank you for all the kindness you have shown me.

The PRESIDENT: I am sure we are all very much obliged to Dr. Row for the information he has given us, and also for the fact that he has been persuaded to leave his laboratory in India to visit us in London. It is the first time this Society has seen him, and, I am sure, all those who are not acquainted with India, and not familiar with the valuable work that is going on there, will be surprised to hear that so much has been done. But nothing is astonishing with Dr. Row, because we are all familiar with his work. I have no doubt he will honour us with a visit in the future, and will tell us something further of the work he is doing. We shall be very pleased to welcome him again. We are very much interested in what he has said, and are indebted to him for his excellent paper.

COMMUNICATION.*

OBSERVATIONS ON THE PATHOGENICITY OF *ISOSPORA HOMINIS*, RIVOLTA, EMEND. DOBELL, BASED ON A SECOND CASE OF HUMAN COCCIDIOSIS IN NIGERIA ;
WITH REMARKS ON THE SIGNIFICANCE OF CHARCOT-
LEYDEN CRYSTALS IN THE FÆCES.

BY

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CONNAL and YOUNG (1922) have reported a case of human coccidiosis in Nigeria, in which the infection was due to *Isospora hominis*, RIVOLTA, 1878, emend. DOBELL, 1919. A second case, now to be described, occurred a few weeks after the first, and the history leaves little room for doubt that it was an example of direct transmission by means of the fæces.

The History.—The stools of the original case were examined by the second patient on 24th, 25th and 30th January, 3rd, 7th, 11th, 14th, 17th, 21st and 28th February, and 7th March, 1922. On the dates from 7th to 17th February inclusive, the oöcysts of *I. hominis* were present in the samples, but they were not seen on the other dates. They were most numerous in the stool passed on 14th February. The usual precautions were taken in making these examinations, and a long glass-handled platinum loop was employed for picking out a small portion of the fæces, the wire being sterilised in the flame immediately after use. On 16th February, a stool which had been kept for two days was being again examined in order to note the development of the oöcysts. These, as noted above, were very numerous, and most of them showed two sporocysts each containing four sporozoites. A quantity of about 30 grammes of this particular specimen of fæces had been well shaken with normal saline in a litre flask, according to the method of CROPPER and ROW for the con-

*With a view to making the TRANSACTIONS more interesting, it is proposed to insert SHORT COMMUNICATIONS from Fellows relative to any matters of medical, sanitary or parasitological interest. It is felt that many Fellows in various parts of the world must be in a position to contribute short papers on these subjects, and the Secretaries will be pleased to receive any such from them.

centration of cysts, and, whilst giving the few shakes necessary after the addition of ether, the flask burst close to the observer's head. Two or three small cuts were inflicted on the lips and chin, and most of the contents of the flask were received over the face. None actually was detected in the mouth, but the lips and nose were freely bespattered. A bath in strong antiseptic (lysol) solution was taken immediately, but the mouth was not washed out. Six days later, on 22nd February, the observer was awakened about 5 a.m. with diarrhœa. The looseness of the bowels persisted thereafter until 24th March, the motions numbering six to eight per day. He examined his stools each day, but it was not until 16th March (twenty-eight days after the bursting of the flask and twenty-two days after the onset of diarrhœa) that oöcysts of *I. hominis* were found. The daily microscopical examination of the fæces was continued up to 29th March, when the patient was invalided home. The presence of oöcysts was recorded each day from 16th to 24th March, on which day none was found. Two days later they reappeared, and they were still present on 27th and 28th March. On 29th March, however, they were absent. No opportunity of examining the stools was again afforded until 17th April. By the kindness of Dr. A. ROBERTSON, a thorough search was then made, and repeated on the four following days, in the Protozoological Department of the School of Tropical Medicine, London. No intestinal protozoa were observed, and a similar result has attended the fairly numerous examinations made up to date (September, 1922).

The Fæces.—During the period 22nd February to 15th March, the stools were, in appearance, such as would be passed after the use of a saline purge. They were liquid and of a brownish yellow colour, containing incompletely digested material. No mucus was observed. Under the microscope there was no blood or pus and no protozoa were seen. From 16th to 22nd March, however, the fæces presented an appearance, to the naked eye, that had not been encountered previously in the experience of the laboratory. They were copious and of a thick oily consistency, showing signs of slow gaseous formation. There were short streaks and small rounded masses of a light primrose-yellow colour in the general brown mass, giving a striking mottled and marbled effect. Whilst, previously, there had been the usual fæcal stench, not unduly offensive, it was now barely perceptible, the odour being rather that of

fermenting matter, and strongly suggestive of stomach contents vomited. Numerous oöcysts of *I. hominis* and large numbers of Charcot-Leyden crystals were observed during this period, but no blood or pus cells, no ova of helminths, and no protozoa other than *I. hominis* were ever seen. The small rounded masses and short streaks were seen to be collections of semi-liquid fat, and, in addition, there was a large quantity of undigested starch and muscle fibre. During the next two days the stools gradually became formed, and, since 24th March, there has been no abnormality in their appearance, excepting that on 26th, 28th and 29th March there was a small amount of mucus adherent to the formed mass. On the first occasion the mucus was grey in colour and stringy. It contained a few epithelial cells in which no forms of the parasite were distinguished. On the other two occasions the mucus was tough and yellowish, with no formed elements in its substance. During the period 23rd to 29th March, the oöcysts became fewer, and on 24th and 25th March they were not seen. On 26th March, however, they reappeared, and they persisted, in small numbers, up to 28th March. Since 29th March no oöcysts have been seen. The Charcot-Leyden crystals did not disappear until the last-mentioned date, but they were much fewer on 24th March, the day on which oöcysts were absent for the first time. The amount of undigested fat, starch and meat fibre gradually lessened, but even as late as the end of April a few signs of incomplete digestion were present.

Differential Diagnosis.—For thirty-six days, *i.e.*, from the beginning of the illness until the last day of the patient's stay in Nigeria, the method of CROPPER and ROW for concentrating cysts in faeces was used with every specimen, and a search through this material was always made, in addition to the usual examination. It may be repeated again, that no pus cells, no erythrocytes, no protozoa other than *I. hominis*, and no helminth ova were ever found and that Charcot-Leyden crystals were present from the day on which oöcysts first appeared until they finally disappeared. After the onset of diarrhoea on 22nd February, it was suspected that the disturbance was most probably due to a coccidial infection, but other causes were also sought for. At intervals, both before and after the coccidia were found, the faeces were plated on various selective media, but on no occasion were organisms of the food-poisoning, typhoid or dysentery groups isolated. The serum, at three

different periods of the illness, was tested against the laboratory stock cultures of FLEXNER's and of SHIGA's bacillus, and the typhoid and paratyphoid bacilli, but no agglutination was obtained. Blood smears were examined from time to time. There were no malarial or other parasites and no pigmented mononuclear leucocytes. There was no increase in the total leucocyte count, the polymorphonuclear neutrophil percentage was never over 55, and the large mononuclear cells were in the proportion of 12 to 14 per cent. Towards the end of the illness, some inequality in the size and the shape of the red cells was observable, but the hæmoglobin percentage, by TALLQVIST's method, was always over ninety. The urine showed no albumen, blood or sugar by chemical tests, and the centrifugalised sediment contained only a few epithelial cells presenting nothing noteworthy.

Signs and Symptoms.—The signs and symptoms were not very prominent or severe. They were diarrhœa, abdominal discomfort, some flatulence later, loss of weight and a certain amount of lassitude. The patient, although unfit for much physical exertion, was on duty throughout the attack, except for one day, 24th March, when, although the fæces had become normal or nearly so, he felt "played out." The character of the diarrhœa has already been described. The abdominal discomfort was limited to an area over the situation of the duodenum. There was no actual pain or tenderness in the abdomen and no distention. Flatulence developed after the diarrhœa abated. The area of liver dulness was not altered and there was no tenderness in this organ or in the spleen, neither of which appeared to be affected. The appetite was neither lessened nor perverted, in fact it increased above the usual, doubtless because of the decreased absorption of food from the irritated bowel. There was no undue thirst. The temperature never rose above 99·8° F., and it reached this figure on only two occasions. Sleep was not interfered with and headache was absent. Recovery was rapid, after 29th March, but it was not until the end of April that the appetite became normal and flatulence abated.

Treatment.—No treatment was administered until after oöcysts were found, on 16th March. Thereafter, a powder containing bismuth salicylate and charcoal was taken thrice daily, and the diet was restricted to easily digestible food, in small amount. Latterly, however, with the ever-increasing appetite, and in spite of the diarrhœa, which was

apparently unchecked by the powder, the ordinary diet was resorted to, except that fats were eliminated as far as possible. It was only after the addition of pulv. opii to the powder that the diarrhoea ceased, and this occurrence coincided with the lessening in numbers and final disappearance of the parasite.

Personal History.—The patient was a European, male, aged 40 years, engaged in laboratory work. He had fourteen years' service in West Africa, and had never suffered from dysentery or other intestinal disease. His medical history sheet contained no entries under the heading of illnesses.

The Parasite.—As regards the oöcysts found in this case, it was noted that, until late in the illness, none of these proceeded to the sporoblast stage on being kept for three days, or longer, at room temperature. It was only in the specimens passed from 26th March onwards, that development proceeded in the usual way, *i.e.*, the formation of two sporoblasts, each becoming a sporocyst containing four vermiform sporozoites. There was nothing in the shape, size or general appearance of the oöcysts at any time, which differed from the description of these forms by WENYON (1915) and DOBELL (1919). They are not figured in this paper because there is nothing to add to the characters already defined.

Remarks on the Case.—Throughout the illness there were no short remissions as are mentioned by Noc (1920) and HAUGHWOUT (1921). The very incomplete digestion, as evidenced by the microscopical examination of the fæces, may possibly be explained by the shortness of the period during which the food was exposed to the action of the intestinal juices, and it is to be regretted that no chemical tests were applied. The localisation of the abdominal discomfort in the region of the duodenum, however, suggests a pancreatic involvement, and this would account also for the digestive deficiency. Or, again, the formation of *succus entericus* may have been impaired, thus affecting its normal chemical interaction with the secretion of the pancreas. In any case, until we know something of the site of the infection, and the nature of the lesions in human coccidiosis, these suggestions must remain highly speculative. It is reasonable, however, to conclude that the illness described in the foregoing pages was due to an infection of the intestine with *I. hominis*. The date of actual exposure to infection may,

conceivably, have been earlier than 16th February, but in view of the peculiar circumstances it is unlikely. Accepting that date as the time of inoculation, the signs of infection appeared six days later. This incubation period appears a short one, having in view the length of the latent period in protozoal diseases generally, but it may have depended, as, indeed, may the whole illness, on the massiveness of the infective dose. It is improbable that, in nature, an individual is exposed directly to such a large number of sporozoites in such a short time, as happened in the present instance. The next period of three weeks was characterised by a persistent diarrhœa, with nothing extraordinary about the stools. But, during the next week, the macroscopic appearance of the fæces was decidedly unusual, consisting of an oily-looking, fermenting, mottled and marbled mass, with no characteristic fæcal odour. During this week oöcysts of *I. hominis* and Charcot-Leyden crystals were numerous and the bulk of the material consisted of undigested food-stuff, fat particles predominating. Thereafter, there was rapid improvement, the fæces became formed, parasites and crystals disappeared and, in a surprisingly short time, the patient felt well. He had, however, lost weight and strength. The probability is that the three weeks period corresponded to the actively propagative stage of the parasite, when reproduction was by schizogony, the second period of a week was associated with the phase when the epithelial host cells were becoming less attractive and sporogony was resorted to, while the third period of a week or longer coincided with the passing out, in the fæces, of the remaining parasites as oöcysts. The definite impression was received that the medicinal treatment had little, if any, influence on the course of the illness.

It has to be borne in mind that the present case may have been and probably was exceptional in its severity, and the decided nature of the attack raises interesting considerations, which have a bearing on the apparent rarity of the condition. For instance, the long period of active diarrhœa during which no parasites were found and the supervening short period in which oöcysts were readily recognized, give some basis for a belief that cases may escape notice. Forming one's impressions of the infection from the present and from other cases, it would seem to be usual that when the oöcysts appear in the fæces, the acute phase of the illness is over. Indeed, DOBELL and O'CONNOR (1921) p. 105, have

anticipated this: "There is nothing to show that the schizogonic cycle can be repeated indefinitely; and the occurrence of oöcysts in the stools may mark the completion of development and the final exit of the parasite." It is conceivable that cases of "Diarrhoea" occur, in which—no parasitic cause having been demonstrated during the first ten days or so—intestinal sedatives have taken effect before the oöcyst-passing stage is reached; the patient would appear to be well and be going about his ordinary duties at a time when a microscopical examination of his fæces might reveal oöcysts. It is significant that practically all the known cases of coccidiosis have been recorded by the protozoologists, not from the bedside but from the laboratory during the pursuit of other research; and it is readily explicable, of course, if the illness be a mild one and if it be the general rule that the oöcyst-passing stage is concurrent with convalescence. The inference is that if cases of "Diarrhoea" were examined over a long period, more instances of coccidial infection might be revealed. It would require patient search, for it has been shown that at least three weeks may elapse before oöcysts are found. But DOBELL (1917) recommends that for the acceptance of a "cure" in amoebic dysentery, the fæces should be examined on at least six occasions during not less than that length of time after the cessation of treatment. Such a procedure might, with advantage, be adopted in tropical and sub-tropical laboratories, for the double purpose. The foregoing considerations may explain the apparent rarity of the disease under discussion. But it must be remembered that, according to DOBELL (1919), there are only five more or less well-authenticated cases of intestinal coccidiosis recorded prior to 1915. Since that year the number has increased to over one hundred. It is safe to say, however, that never before that date, in the whole history of medicine, have so many samples of fæces from so many persons been examined by such a large number of trained observers. These factors, alone, might well explain what would otherwise seem an astonishing increase in the prevalence of coccidiosis. There are those who hold, however, that the infection has been endemic in a comparatively restricted and little investigated area, usually alluded to as the Eastern Mediterranean, including Gallipoli, Salonika and parts of Egypt and Mesopotamia. They believe, also, that it was the enormous influx of combatants and non-combatants to this area that led to the increase in the number of

cases and to the spread of the disease to such widely separated places as the United States of America, the Dutch East Indies, the Philippine Islands and Africa. The geographical distribution is, indeed, now world-wide, although prior to 1915 the known cases of intestinal infection were confined to Western Europe, three in Germany and two in France.

Notes on the Cases Previously Recorded.—Although most of the authorities (WENYON 1915, 1916, DOBELL 1917, 1919, WENYON and O'CONNOR 1917, O'CONNOR 1919, DOBELL and O'CONNOR 1921) are agreed that both *Isospora* and *Eimeria* are potentially pathogenic organisms and that they are at times the cause of grave disease in the lower animals, they point out that they are frequently found, even in enormous numbers, in animals which show no signs of illness. They add that, as yet, there is no proof of the pathogenicity of the intestinal coccidia in man. In the light of the knowledge gained from a consideration of the present case, it was thought advisable to analyse the reports of those previously published, particularly as PORTER (1918), NOC (1920), and HAUGHWOUT (1921) have described human cases of the infection, in which they believe that certain ill-effects were due to the parasite. The recorded cases can be conveniently examined in their chronological order. DOBELL (1919), as already noted, reduced the number of authenticated, pre-war cases to five. These, leaving out the cases of hepatic coccidiosis, are included in the following table, which takes note of the observers, the year of publication, the locality in which the cases occurred, and the number of cases:—

NAME.			YEAR.		PLACE.		ISOS.	EIM.
Kjellberg (Virchow)	...	...	1860	...	Germany ...	...	1	—
Eimer	...	...	1870	...	"	...	2	—
Raillet and Lucet	...	...	1890	...	France ...	...	2	—
Woodcock	...	...	1915	...	England. from	E.M.	5	—
Low (Wenyon)	...	...	1915	...	"	"	1	—
Wenyon	...	...	1915	...	"	"	—	1
Woodcock and Penfold	...	...	1916	...	"	"	5	—
Dobell	...	...	1916	...	"	"	1	—
Wenyon	...	...	1916	...	"	"	15	—
Dobell and Stevenson	...	...	1916	...	"	"	1	—
Fantham	...	...	1916	...	"	"	4	—
Williamson	...	...	1917	...	"	"	2	—
Roche	...	...	1917	...	E.M.	...	15	3
Richards	...	...	1917	...	"	...	18	—
Wenyon and O'Connor	...	...	1917	...	"	...	1	—
Savage and Young	...	...	1917	...	"	...	6	—
Castellani	...	...	1917	...	Macedonia	...	? 6	—

NAME.	YEAR.	PLACE.	ISOS.	EIM.
Cragg	1917	Bombay, from E.M.	1	
Boney, Crossman and Boulenger ...	1918	E.M. ...	7	
Martin, Kellaway and Williams ...	1918	" ...	1	
Porter	1918	Johannesburg ...	2	
Sangiorgi	1918	Italy ...	1	
Chatton	1918	Tunisia ...		3
Mesnil	1918	From Dardenelles ...		1
Roubaud (Mesnil)	1918	In armée d'Orient ...	1	
Low (Dobell)	1919	England ...		1
Gunn and Savage	1919	E.M. ...	8	
O'Connor... ..	1919	" ...	9	
Kofoid, Kornhauser and Plate ...	1919	New York ...	8	
Kofoid and Swezy... ..	1920	" ...	3	
Noc	1920	Saigon and Dakar ...	2	
Snijders	1920	Medan ...		1
Thomson (Thomson and Robertson) ...	1921	E.M. ...	11	
Thomson and Robertson	1921	England ...	1	
Haughwout	1921	Manila ...	1	
Brug	1922	Batavia ...	1	
Connal and Young	1922	Nigeria ...	1	
Broughton-Alcock and Thomson ...	1922	England ...		1
Newham (Newham and Robertson) ...	1922	East Africa ...	2	
Newham and Robertson	1922	(England, from South Africa ...	1	
Connal	1922	Nigeria ...	1	
Totals ...			153	11

In addition to the above there are some cases which are of an indefinite nature, and others of mistaken identity. CASTELLANI (1917) states that "coccidiosis is, comparatively speaking, common in the Balkans." PORTER (1918) states, p. 44: "Of these two organisms [Isospora and Eimeria] I have found Isospora both in stools and at post-mortem examinations." As both the South African of Dutch descent and the Hottentot were not noted as having died, it must be assumed that other cases are referred to. LOCKHART-MUMMERY and GABRIEL (1919) reported a case of intestinal coccidiosis (?) which DOBELL (1921) has shown was due neither to a coccidium nor any other protozoon. HUETTER (1919) described a case of rectal tumour in which he found coccidia, but the same author (1921) admits that the structures were Oxyuris eggs.

It may be added that BRUMPT (1918) states that "Isospora oöcysts occur in 0.4 to 4 per cent. of dysentery cases and those of Eimeria in 0.2 to 0.33 per cent." He also states that coccidia "seem to be pretty common in dysentery convalescents." It is not clear that these figures are founded on the work of the British observers.

In the following brief analysis, except where otherwise stated, the findings were based on the examination of British soldiers suffering or having suffered from intestinal disease, mainly dysentery, contracted in Gallipoli, Salonika, Egypt or Mesopotamia (grouped for the purposes of this paper into the Eastern Mediterranean Area), and referred to in the table as E.M.

WOODCOCK (1915) commenting on five cases of infection with *I. hominis*, notes that the oöcysts were scanty in four and not infrequent in the fifth.

LOW (WENYON 1915) found one case of *I. hominis* at the Royal Albert Docks. WENYON (1915, 1915a, 1915b, 1915c) mentioned the occurrence of cases of human coccidiosis, described the development of the oöcyst of *I. hominis* and recorded the finding of *Eimeria wenyoni* (DOBELL 1919).

WOODCOCK and PENFOLD (1916) continuing WOODCOCK's earlier work, found other five cases of *I. hominis*, in all of which the parasites were scanty. They add: "there was no sign of pathogenicity in connection with their presence."

DOBELL (1916) found oöcysts of *I. hominis* in the fæces of one case.

WENYON (1916) noted fifteen cases of infection with *I. hominis*. In most, the infection "was quite small, but in one, in which an accompanying small *Entamoeba coli* infection occurred, the oöcysts were present in very large numbers." Ten and twenty days later no oöcysts were found. He adds: "It may have been that the dysenteric symptoms of this case were due to the coccidium, for no pathogenic bacteria had been isolated from the fæces."

DOBELL and STEVENSON (1916) found a case of *Isospora* in which "the stools were examined—sometimes most exhaustively—on six occasions, and only a single oöcyst was ever found."

FANTHAM (1916) reported four cases of *Isospora*.

ROCHE (1917) found fifteen cases of *Isospora* and three of *Eimeria*. He states that "where this infection [coccidiosis] occurred, mucus was always present in the stools" and that "as a rule these parasites [coccidia] disappeared within a few days, but in one patient they were found in daily examinations for three weeks."

IMRIE and ROCHE (1917) supply details of a case which is probably the same as the one last-mentioned. The infection was mixed, *i.e.*, *E. histolytica*, *E. coli* and *Lambliia intestinalis* were present in addition to

I. hominis. Oöcysts were found on 8th, 17th and 24th August, but not on 23rd, 30th, or 31st August or at daily examinations from 2nd September to 14th October.

WILLIAMSON (1917) found *Isospora* in 2 cases.

WENYON and O'CONNOR (1917) found *Isospora* at the eighth examination of a healthy carrier of *E. histolytica*. The oöcysts, at first few in number, increased during a first course of emetine, persisted throughout the interval and only disappeared on the sixth day of a second course. All examinations were negative for a month thereafter. They add: "There were no symptoms attributable to either the *E. histolytica* or the *Isospora*. If he contracted the infection in Gallipoli, he must have carried it seven months."

CRAGG (1917) found four cases of *Isospora* in Bombay. Two died, one of amœbic, the other of bacillary dysentery. The third case was examined four times, *Isospora* being found once. The fourth case had previously suffered from dysentery and from diarrhœa and had not passed a normal stool in five months. He was examined four times in three weeks. Mucus was always present and also much undigested food. Oöcysts were found at the first and third examinations and no other protozoa were noted.

SAVAGE and YOUNG (1917) found *Isospora* in six cases. Five of these were in hospital, two with acute and one with chronic amœbic dysentery and two with bacillary dysentery. In one of them, the oöcysts disappeared after three days, re-appeared after eleven days, and were not seen again during sixteen days in a series of daily examinations.

CASTELLANI (1917) mentions that he saw six cases of coccidiosis in Macedonia (the nationality of the patients is not stated). There was diarrhœa in two and the others did not show any intestinal symptoms. He also alludes to cases described by Capt. RICHARDS. Dr. C. M. WENYON kindly communicated with Capt. RICHARDS who was good enough to send information from which the following has been extracted:—

RICHARDS (1917, unpublished thesis) found eighteen cases of *Isospora* at Salonika. In ten, coccidia only were found; in two, there were also *B. dysenteriae*, FLEXNER; in one, *B. dysenteriae*, SHIGA; in one, *Chilomastix*; in one, *Trichomonas*; in one, *E. coli*; in one *B. paratyphosus* B; and in the last, the ova of *Tricocephalus dispar*. In two

the stools were normal; in nine they were brown unformed; in one (with *Trichomonas*) they were brown liquid; and in six they were brown, unformed or liquid with obvious mucus. In three cases the coccidia were present in enormous numbers.

The dominant symptoms in all were diarrhoea, with abdominal pain or discomfort. The diarrhoea was severe in only three cases, in two of which there was bacillary dysentery. There was a history of recurring attacks of diarrhoea and constipation, and, in practically all, there was a history of passing mucus. The abdominal pain was not severe, apart from the true dysentery cases, and was described frequently as uneasiness or discomfort only. In most cases there was associated a feeling of physical weakness and several gave a history of being out of sorts, with irregularity of the bowels for some time before declaring sick. "The occurrence of alternating constipation and diarrhoea, with mucus and slight abdominal pain and debility, is considered worthy of record."

MARTIN, KELLAWAY and WILLIAMS (1918) found *Isospora* in one case and they state that "no grounds were discovered for supposing that the protozoological parasites, other than *Amœba histolytica*, were responsible for ill-health."

PORTER (1918) found two cases in Johannesburg. In one, a Hottentot, the infection was heavy, and *E. coli* and *Cercomonas parva* were also present. The other was in a South African of Dutch descent. "His condition was at first thought to be due to amœbic dysentery, but *I. bigemina* var. *hominis* was the only protozoon present, and, with its destruction and elimination, the symptoms also disappeared."

BONEY, CROSSMAN and BOULENGER (1918) met with seven cases of *Isospora*. "No special symptoms of coccidiosis were, however, noted in any of these."

SANGIORGI (1918) reported a case of nephritis in a soldier. He found stages of *Isospora* in the urine and oöcysts in the fæces. In a footnote he adds that the clinical account is to be contributed by Dr. S. GANTI. (This publication has not been seen.)

LOW (1918) described a case of amœbic dysentery in which *Eimeria oxyspora*, DOBELL, 1919, occurred. DOBELL examined the fæces most exhaustively on over forty occasions in the course of a year, but the oöcysts were found only once.

CHATTON (1918) found three cases of *Eimeria* in South Tunisia.

The first two were noted in 1916. Both had enteritis, and both were examined again ten days later, with positive results. The third case was found in 1917. MESNIL (1918) found a case of *Eimeria* in a soldier from the Dardenelles. ROUBAUD (MESNIL, 1918) noted a case of *Isospora* in a soldier from the "armée d'Orient."

O'CONNOR (1919) found seven cases of *Isospora* in British soldiers, in addition to one amongst the Indian troops and another in the Egyptian Labour Corps. In two of the British the infection was heavy. The first complained of no symptoms which could be attributed to the parasite. The second had not been out of England until January, 1916. He proceeded direct to Egypt, and four weeks later complained of a dull pain in the epigastrium and right hypochondrium, and also of a feeling of nausea, which was worse after food. The tongue was slightly coated, and the abdomen was distended with flatus. There was slight tenderness at the lower end of the liver on the right side. During a twelve days' course of emetine, and for three weeks thereafter, there was no change in the physical condition or in the number of oöcysts passed. (This seems to rule out amœbic hepatitis.) He adds: "There is no conclusive evidence that *I. hominis* is, or is not pathogenic."

DOBELL (1919) brought the literature of coccidiosis up to date, eliminated the unacceptable cases, defined the genera *Isospora* and *Eimeria*, described *I. hominus*, *E. wenyoni*, and *E. oxyspora*, and added that there is probably another *Eimeria*, a hepatic coccidium.

SAVAGE (GUNN and SAVAGE, 1919) reports the finding of three cases of *Isospora* in 1917 and of five in 1918.

KOFOID, KORNHAUSER and PLATE (1919) found six cases of *Isospora* among over-seas troops and two among home-service troops.

KOFOID and SWEZY (1920) add another case in over-seas and two more in home-service troops.

SNIJERS (1920) found the oöcysts of a new *Eimeria* in the fæces of a man suffering from chronic relapsing amœbic dysentery, in Medan, Sumatra. They were found only once in numerous examinations. The particular specimen contained no blood or mucus. He states that "the pathogenic power, if present, is of little importance" and that "either the formation of an appreciable number of cysts very seldom occurs, or the infection is most transitory."

DOBELL (1920) described SNIJERS' *Eimeria* as *E. snijdersi*.

Noc (1920) found scanty oöcysts in the fæces of a European at Saigon, who suffered from diarrhœa, but who was examined only once. He also describes a case of intestinal coccidiosis in a discharged French soldier in Dakar, French West Africa. He had been a prisoner-of-war in Germany, during which time he suffered much from diarrhœa. A year after arrival in Dakar he developed diarrhœa. A month later, on examining the fæces, oöcysts of *I. hominis* and cysts of *L. intestinalis* were found, also crystals which from their description were probably Charcot-Leyden. No dysentery bacilli were isolated. Novarsenobenzol intravenously and thymol by the mouth were given. Fifteen days later the parasites were fewer in number. In some epithelial cells in the fæces Noc saw what he took to be developmental forms of the parasite, also larger structures, extra-cellular, considered to be further stages of *I. hominis*. A month after the first examination, diarrhœa having ceased, no parasites were found. The signs of the illness were loss of weight, pain in the right iliac fossa and enlargement of the liver, with diarrhœa characterised by three to four liquid, evil-smelling stools daily. There were short remissions of twenty-four hours. A slight increase in the mononuclear leucocyte percentage was the only abnormality in the blood. Noc considers that his patient's illness was due to *I. hominis*.

HAUGHWOUT (1921) describes a case in an American chemist in Manila. He was under observation forty-one days and the fæces were examined on eight occasions. At the second examination one oöcyst of *I. hominis* was found, at the third several were seen, and at the fourth, fifth and sixth they were numerous. At the seventh none was observed but at the eighth there were again a few oöcysts present. At the first examination, about four weeks after the onset of diarrhœa, numerous small amœbæ, not identified, were found and at the third examination Charcot-Leyden crystals were noted. He suffered from diarrhœa, looked ill and lost weight. There were anorexia, nausea, abdominal discomfort and flatulence. The tongue was usually foul. The stools at times were watery but always fæculent. They contained "no pathologic elements aside from shed epithelial cells." HAUGHWOUT did not find intracellular stages in these. There appeared to be a "tertian periodicity, on one day the stool would be normal, the next day soft and watery, and on the following day normal, and so on." HAUGHWOUT attributes the patient's illness to *I. hominis*.

THOMSON (THOMSON and ROBERTSON, 1921a) in Egypt found eleven cases of *Isospora*, four in 1915, six in 1916, and one in 1917. One of these had *E. histolytica* in the stools, two had mucus and degenerated epithelial cells but no *E. histolytica*, and the remainder had, other than the oöcysts of *Isospora*, no abnormality either macroscopically or microscopically. Cultures were negative to the bacillary group of organisms.

THOMSON and ROBERTSON (1921) note that "one stool received from Dr. BROUGHTON-ALCOCK contained, in addition to numerous Charcot-Leyden crystals, the oöcysts of *I. hominis*, and it was only after a prolonged search that a free vegetative *Entamoeba* of undetermined species was found. Unfortunately we were unable to pursue the case further."

BRUG (1922 and 1922a) examined the stools of 3,458 persons in Batavia during 1917-1920. He found a single *Isospora* oöcyst in one case. During 1921 he found three cases. The first was in a half-caste, aged $2\frac{1}{2}$ years, who developed diarrhoea in hospital. A few active *E. histolytica* and many *Isospora* oöcysts were found. The amœbæ disappeared under emetine, but the oöcysts persisted. Their number, during an observation period of about six weeks, varied greatly, but they were seldom absent. A few months later the child returned to hospital with diarrhoea, which cleared up after santonin had been given for an *Ascaris* infection. During a month's observation thereafter, only one (degenerated) oöcyst was seen. The second case was in a small child who was in the same ward at the same time as the first. BRUG thinks there was possibly some connection between the first and the second. The third case was in a servant who worked in another ward. All three persons had never been out of the country. BRUG mentions the phenomenon of coccidiosis in rabbits, causing little or no harmful effects over a period, and then suddenly developing considerable pathogenicity. He suggests that this might also occur in human coccidiosis.

CONNAL and YOUNG (1922) report a case from Nigeria in a European. There was a history of frequent attacks of diarrhoea. The fæces were examined on eleven occasions in six weeks. One oöcyst of *I. hominis* was seen at the fifth examination. Oöcysts were numerous at the sixth and seventh, but were few at the eighth examination, and they were not again found. Some doubtful and degenerated *E. histolytica* were observed at

the second examination, but they were not seen in other specimens. Charcot-Leyden crystals were usually present. Epithelial cells were also usually found, but no intracellular stages were noted. The patient looked ill, and was confined to bed. He lost weight. CONNALL and YOUNG consider the case was one of chronic amæbic dysentery.

BROUGHTON-ALCOCK and THOMSON (1922) found oöcysts of *E. oxyspora* in a specimen of human fæces in England. They occurred in one specimen only, and were not found seven days previously or eleven and fifteen days afterwards. The number of fat particles in the fæces was an outstanding feature.

NEWHAM (NEWHAM and ROBERTSON, 1922) reports two cases of *Isospora* infection met with during the campaign in East Africa. One occurred in a nursing sister, who had previously been in the Eastern Mediterranean. The oöcysts were found in the stools during her convalescence from paratyphoid fever. The other occurred in a Portuguese soldier, three months after his arrival from England. He had attacks of diarrhoea lasting two days, recurring every ten days or so. Both cases are regarded as having been contracted in East Africa.

NEWHAM and ROBERTSON (1922) describe the case of a lady who had spent two years in South Africa. During the voyage back to England she had several "dysentery" attacks. On arrival in London the stools were examined. They were soft, semi-solid, light brown, not unduly offensive, and with a "rather fermentative appearance." *Isospora* oöcysts, Charcot-Leyden crystals, and a few *Chilomastix mesnili* were found, but no amœbæ, blood or pus cells. The greater proportion of the oöcysts showed no further development after the stool was passed. Only one specimen of fæces was obtainable.

Remarks.—The earlier workers agree that there is no evidence that the human coccidia are pathogenic. On the facts supplied, this opinion is justified, for, in cases where signs of illness were present, it was impossible to eliminate causes such as *E. histolytica*, the dysentery bacilli or the typhoid group. In the few cases where these could be excluded, there were apparently no signs of illness. Neither was there any constancy in the findings, for in some cases the oöcysts were few, in others numerous; in some they persisted for weeks, in others they rapidly disappeared or were found only once. CASTELLANI (1917) apparently considered coccidia pathogenic as he mentioned that two of his cases

had diarrhoea and that coccidiosis is difficult to treat. He supplies no details of signs or symptoms. RICHARDS (1917) in his valuable personal communication, attributes pathogenicity to *Isospora*. PORTER (1918) attributed a dysentery-like attack in a South African to *Isospora*, but details are lacking. NOC (1920) and HAUGHWOUT (1921) furnish particulars of cases, in both of which the evidence strongly favours the view that *I. hominis* was the pathogenic agent. It is probable, too, that the demonstrated *Isospora*, rather than the doubtfully determined amœba in CONNALL and YOUNG'S (1922) case, was the cause of the illness. It is to be noted also that two of the cases described by NEWHAM and ROBERTSON (1922), the Portuguese soldier and the lady from South Africa, suffered from marked intestinal disturbance. The case which forms the basis of this paper, however, offers the clearest proof of the pathogenicity of *I. hominis*, and the nature and progress of the illness lead one to the belief that several of the earlier cases, *e.g.*, WENYON (1916), CRAGG (1917) fourth case, and O'CONNOR (1919) second case, were instances of intestinal disorder due to *Isospora*. A consideration of the foregoing epitome, shows also that in many, particularly the *Eimeria* infections, the pathogenic effects are extremely slight or absent altogether. It is obvious, then, that the human coccidia, like those of the lower animals, may or may not, and usually do not produce noticeable signs of illness.

Methods of Treatment.—Several drugs have been tried, such as emetine, both hypodermically and by the mouth, alcrestal, thymol and methylene blue internally, and novarsenobenzol intravenously. It cannot be claimed that any has proved successful or even beneficial. The lines known as "expectant" may be followed with advantage, and symptoms relieved as they arise, in the present belief that the disease is comparatively mild and is self-limiting.

Occurrence.—HAUGHWOUT (1921, 1921a, 1921b) fears that the infection may spread and that its prevention may be a problem added to the task of the sanitarian. It has been shown that an infected person may pass oöcysts in his faeces over a period of several weeks. The oöcysts are probably extremely resistant, and would thus be difficult to render harmless. Regarding the possibility of spread, the literature shows how remarkable has been the occurrence of the human coccidia. There were five cases of *Isospora* between 1860 and 1890. After a lapse of twenty-five years and within the short space 1915-1918 over 100 cases

were reported, practically all in British soldiers in the Eastern Mediterranean. The group of workers in England, whose duty it was to examine the faeces of cases in the military hospitals, invalided from that area, WOODCOCK (1915), WOODCOCK and PENFOLD (1916), DOBELL (1916), DOBELL and STEVENSON (1916), FANTHAM (1916), WENYON (1916), WILLIAMSON (1917) and others, in many thousands of cases examined, found *Isospora* oöcysts in thirty-three and *Eimeria* in one. The workers in the Eastern Mediterranean, ROCHE (1917), SAVAGE and YOUNG (1917), WENYON and O'CONNOR (1917), RICHARDS (1917), BONEY, CROSSMAN and BOULENGER (1918), MARTIN, KELLAWAY and WILLIAMS (1918), GUNN and SAVAGE (1919), O'CONNOR (1919), THOMSON (THOMSON and ROBERTSON, 1921) and others, in about 20,000 cases found *Isospora* in seventy-six and *Eimeria* in three. Other cases which probably had some connection with this particular area are those of LOW, MESNIL, ROUBAUD, CRAGG, CHATTON and SANGIORGI and also CASTELLANI. The other cases, from 1918 onwards, show no direct connection with the Eastern Mediterranean, although those found by KOFOID and his co-workers may have had an indirect association. The case from Dakar and the case from Manila had contact, one direct the other indirect, with the war in Europe, but the interval in each case was long. The Batavian and Johannesburg patients had not been out of their respective countries. In spite of at least thirty-three opportunities the infection has not spread in England. DOBELL (1919) mentions that no cases have been found here since 1916. This has been corroborated by other workers, DOBELL and JEPPE, CARTER, MACKINNON, MATTHEWS and SMITH, TURNER and TAYLER, BAYLIS and others, up to 1921. Nor, though less exhaustively ascertained, have cases occurred in other European countries. The cases since 1918 (with the doubtful exception of DOBELL and Low's 1918 and BROUGHTON-ALCOCK and THOMSON's 1922 *Eimeria* cases and THOMSON and ROBERTSON's *Isospora* case, in 1921), have all occurred in tropical or sub-tropical countries. It is in these cases too, that more or less definite signs of illness have been noted. Apparently then, a warm climate and inefficient sanitary arrangements favour the development of the coccidia just as they do the other intestinal protozoa.

It seems likely that a restricted focus of the infection was disturbed in the early days of the war, and the world-wide intercourse led to its

being carried to different parts of the globe, where at a few isolated points it found favourable conditions.

Nevertheless it may be that, as with *Endolimax nana* or *Iodamoeba bütschlii*, for instance, common intestinal protozoa only require to be clearly and definitely described in order to be recognised, and that, as already mentioned, cases of coccidiosis may be missed because of the lack of indication for an examination of the fæces, or because oöcysts appear only after the acute signs of illness have abated.

The significance of Charcot-Leyden Crystals.—THOMSON and HIRST (1918), describing the stools in entamœbic dysentery, come to the following conclusions: "A very common feature is the presence of Charcot-Leyden crystals caused by the breaking down of the red cells by the action of the entamœbæ. Charcot-Leyden crystals, although not pathognomonic of amœbic dysentery, are, in our experience, very suggestive of the condition, and we have noted their frequency in cases of cyst-carriers with no obvious blood in the stools." THOMSON and ROBERTSON (1921 and 1921a) make further reference to the subject. After quoting various authorities on the occurrence of these crystals in the stools in helminthic cases, they state: "from our own observations on this subject, it is certain that Charcot-Leyden crystals occur in the stools of human cases suffering from entamœbiasis, from which all possibility of a super-imposed helminthic infection has been excluded; it yet remains to be proved that they may occur in helminthiasis *per se*." They also quote ACTON (1918) as stating: "that a very high degree of association exists between *E. histolytica* and Charcot-Leyden crystals, that they do not occur in infections with intestinal entozoa, and that, in the absence of amœbæ their presence is indicative of amœbic colitis." They conclude (1921a) that, amongst other conditions, "human coccidiosis must be studied and, if Charcot-Leyden crystals happened to appear in the stools, prolonged search must be made to decide on the presence or absence of *E. histolytica*." In the present case, the findings were shortly as follows, the fæces were examined every day for a period of thirty-six days. On 16th March, oöcysts of *I. hominis* and Charcot-Leyden crystals appeared together. Neither had been found during the previous three weeks nor were any amœbæ seen. The crystals persisted until 28th March, after which date neither they nor the oöcysts were again seen. On 25th March no oöcysts were noted and the crystals were few. No

other protozoa were ever observed, nor any helminths or their ova. Neither emetine nor any other preparation of ipecacuanha was taken. No blood was observed. In view of the theories as to the derivation of the crystals, it may be noted that the fæces contained much fat.

Summary.—A case of intestinal coccidiosis in a European, in Nigeria, is described. The infection, which was contracted as the result of an accident in the laboratory, was probably an exceptionally severe one.

The incubation period is noted as six days, the onset as sudden, the duration as rather over a month, and the cure as spontaneous.

The signs and symptoms were diarrhoea, abdominal discomfort, flatulence, lassitude and loss of weight.

Oöcysts were present in the stools for nine consecutive days, were not seen on the tenth, re-appeared on the eleventh and twelfth days, and were not found again.

During the first three weeks of the illness no oöcysts were found.

The acute signs of illness abated within one week of the finding of the oöcysts.

Charcot-Leyden crystals appeared and disappeared with the oöcysts. No cause, apart from *I. hominis*, could be found for the illness.

The remarkable feature about the fæces was the large amount of undigested material, particularly fat.

A review of most, if not all, of the published cases is given. Attention is drawn principally to the occurrence of diarrhoea, abdominal discomfort, flatulence and undigested matter in the fæces.

The conclusion is reached that *I. hominis* is pathogenic to man, and that, whilst in some cases, particularly the one described, it gives rise to illness, it may and probably does cause no obvious disturbance in the majority of cases.

It is a great pleasure to acknowledge the help in obtaining references which was received from Mr. CLIFFORD DOBELL, National Institute for Medical Research, Dr. C. M. WENYON, Wellcome Bureau of Scientific Research, and Capt. R. L. SHEPPARD, Tropical Diseases Bureau.

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* These works were not consulted in the original.

NOTES ON CURRENT LITERATURE.

WATER CHLORINATION.

The chlorination of water is a method of purification which undoubtedly has a future before it in the tropics. Hence it is well to see what the greatest living medical authority on water-supplies has to say regarding it. Sir ALEXANDER HOUSTON, in his last report to the Metropolitan Water Board,* has a section entitled "Some General Notes on the Future of Chlorination." He prefaces his remarks by these two statements:—

"(i.) The typhoid bacillus is believed to be the cause of typhoid fever and is a microbe more easily killed than *B. coli*.

"(ii.) The destruction of *B. coli* by means of chlorination is readily carried out, and the process is exceedingly cheap, both as regards capital outlay and working costs."

He then deals with the three main objections to the method. The first of these is that many persons dislike drinking "doped" water. HOUSTON has no wish to flout sentimental considerations, but he pleads for a sweet reasonableness in the matter, pointing out that if an impure water, like that of many rivers, must be drunk, the innocuous character of the "finished product," rather than its antecedents, should be considered. He states that there is absolutely no convincing evidence that a properly chlorinated water is in any way injurious to health.

The second objection, that chlorinated water sometimes has a most unpleasant taste, is a serious one and, save under emergency conditions, cannot be ignored. In some cases it is quite easy to chlorinate water without imparting to it an unpleasant taste; in others, it is difficult; but it appears to be a fact that by a process of super-chlorination and de-chlorination the trouble can now be successfully overcome. The addition of the permanganate treatment to chlorination often gives a satisfactory result.

*HOUSTON, Sir ALEXANDER. 1922. Metropolitan Water Board. Sixteenth Annual Report on the results of the Chemical and Bacteriological Examination of the London Waters for the twelve months ended 31st March. 1922.

The third objection is due to the fact that the very success of chlorination is apt to encourage "short-cuts to purity." HOUSTON says:—

"How far it is permissible to gamble on the apparent safety conferred by chlorination as an excuse for an otherwise inadequate filtration plant is matter for controversy. The "chlorinators" say, if safety is to be judged by destruction of *B. coli*, no filtration system alone can compete with filtration *plus* chlorination, or indeed with chlorination *per se*, provided the treatment is properly carried out. The "anti-chlorinators" contend that the evidence in favour of the typhoid bacillus being the cause of typhoid fever is not absolutely convincing, and therefore that reliance should be placed on the old filtration processes which have hitherto enjoyed so honourable a past in controlling the spread of water-borne diseases. These matters are, no doubt, debatable, but the writer feels nevertheless that chlorination has a great future before it."

He indicates how it may save pumping charges and be useful under adverse weather conditions; how it has greatly extended our available sources of water supply and how it has many occasional uses as, for example, in time of floods. He discourses on its value in what he calls local treatment, *i.e.*, to supplement a defective filter or to treat water lying on the top of filter beds, and deals with it from the economic aspect. In this last connection he points out that more rapid filtration, *plus* chlorination, is safer bacteriologically than a slower rate of filtration, *minus* chlorination.

The methods of administering chlorine to water are then considered. Under the heading "Gaseous," the form of apparatus employed is discussed, together with the *rationale* of its operation.

HOUSTON believes that the gas is best discharged into the water to be chlorinated in the form of a solution, and insists on the necessity for the perfect mixing of the solution and the water into which it is discharged. A baffle or sluice below the point of application materially aids the process.

He speaks highly of the plants supplied by the Paterson Engineering Company, Limited, and the United Water Softeners, Limited, and mentions that the apparatus (Wallace & Tiernan patents) employed by the latter firm can be used for de-chlorinating water by means of liquefied sulphurous acid gas.

As regards chlorine in the liquid form HOUSTON is most familiar with "Chloros," an alkaline hypochlorite solution containing about 12 to 14 per cent. of available chlorine. He mentions the convenience of liquid chlorine, and as regards relative prices says:—

"Chloride of lime and liquid chlorine are close competitors in the matter of price. Chloride of lime containing about 33 per cent. of available chlorine costs £16 6s. 8d. a ton, or $5\frac{1}{4}$ d. per lb. of available chlorine. Liquid chlorine is, of course, of 100 per cent. strength, and it costs about 4d. per lb. If chloros contained 14 per cent. of available chlorine, its price per 0.1 gallon (=1lb.) would, assuming approximately equal costs as regards carriage, etc., have to come down seemingly to about $\frac{3}{4}$ d. to compete commercially with, say, chloride of lime."

Chloride of lime is then considered, and a plant for using it on a large scale is described. One point only need here be noted, namely, that it has been proved that if the storage tanks holding the solution are covered it will maintain its strength for a much longer period than if the tanks are open.

In the Tenth Annual Report of the Medical Department of the United Fruit Company, from which useful extracts appear in the *Journal of Tropical Medicine and Hygiene*,* there are simple directions for a rough and ready method of chlorinating water which may be given here, although it must be remembered that unless the process is controlled by an appropriate colour test the results may not be altogether satisfactory.

After stating that the bleaching powder must be stored in an air-tight tin or well-stoppered bottle in a dark place, there is a note that a stock solution should be prepared once in six days and kept in a tightly-stoppered coloured bottle. The stock solution is made by dissolving half a level teaspoonful of chlorinated lime in a pint of water. Of this solution use one teaspoonful to two gallons of water, 36 drops to one gallon, or 9 drops to one quart, and let the water stand half an hour before using it.

Of more importance, indeed of very considerable significance, is a reference in the *British Medical Journal* of October 14th, 1922,† to the

* 2nd October, 1922. *Journal of Tropical Medicine and Hygiene*. Vol. 25. No. 19. P. 314.

† 14th October, 1922. "The War Section of the Royal Society of Medicine." *British Medical Journal*. P. 690.

researches recently carried out at the Royal Army Medical College, Millbank, with a view to finding some method of rendering bleaching powder stable in a hot climate. The work has, fortunately, been crowned with success, and it has been proved that by mixing 20 parts of quicklime and 80 parts of bleaching powder a product is obtained which will withstand tropical climates without deterioration, that is to say, it will not lose its available chlorine to any extent. An example is given of a specimen of this stabilised bleaching powder which contained 25.2 per cent. of available chlorine when sent out to West Africa. There it was stored under ordinary conditions for a year, and at the end of that time was found to contain 24.4 per cent., the slight loss being negligible for practical purposes. Some similar results have been obtained in samples sent to Mesopotamia. Here, therefore, we have an important development in water purification, and the method has the advantage of being exceedingly cheap.

The disastrous result of an arrest of chlorination for a single day in the case of a community which derived its supply from a polluted river is reported from California.* The town concerned was Pittsburg, and the river the Sacramento. During repairs the operation of the plant was suspended and unchlorinated water supplied for a day. In consequence there occurred amongst the population of 5,000 one hundred cases of enteric fever and a considerable number of other water-borne diseases. This points to the desirability of installing, whenever possible, a duplicate plant.

ULCERATING GRANULOMA.

Recently, renewed interest has been manifested in the above condition, chiefly because cases of the disease have been cropping up in the United States.

It would seem from a review of a paper in the useful publication of the Medical Research Council, entitled *Medical Science*, that SYMMERS and FROST were the first to draw attention to its occurrence, and that their observations stimulated RANDALL, SMALL and BEEK† to institute an enquiry which resulted in the discovery of seven cases in the Philadelphia General Hospital under wrong diagnoses. The abstractor

* July, 1922. Conséquences de l'arrêt d'un jour dans la chlorination de l'eau de distribution (à Pittsburg). *Office International d'Hygiène Publique*. Vol. 11. No. 7. P. 870. Résumé of article in *Engineering News Record*, 30th December, 1920. P. 1288. Repeated from *Revue d'Hygiène et de Police Sanitaire*. November, 1921. Vol. 43. P. 987.

† RANDALL, A., SMALL, J. C. and BEEK, W. P. September, 1922. "Granuloma inguinale." *Medical Science Abstracts and Reviews*. Vol. 6. No. 6. P. 488.

adds that, to his knowledge, the same is sometimes true as regards London hospitals, to which cases come from warm climates.

The American authors succeeded in cultivating from the sores an encapsulated bacillus, which is apparently the organism described by DONOVAN, and which they consider to be of the *Bacillus mucosus capsulatus* type. Their only success with animal inoculations was in the case of cutaneous inoculation in rabbits when they were able to produce focal lesions, which, however, did not resemble the characteristic sores seen in man.

Like others, they found intravenous treatment with antimony effective.

According to a paper in Spanish, by ITURBE and GONZALEZ,* of Caracas, Venezuela, reviewed by SCOTT in the *Tropical Diseases Bulletin*, granuloma venereum is usually a post-traumatic complication occurring after circumcision or opening a bubo.

Doubt, however, is thrown on the correctness of such a view when we find that PAROUNAGIAN and GOODMAN†, of New York, report a case where the lesions, far from being confined to the inguinal region, were present on the upper lip, the side of the neck, the groin and the anus. The diagnosis was confirmed by the discovery in smears from the ulcerated areas of short bacillary forms resembling DONOVAN's bodies, as well as intracellular forms.

Special interest attaches to the case in that the patient was a white man who was born and had lived all his life in New York City. There is nothing to indicate how the patient acquired infection, but he had a history of a penile lesion six years before, and undoubtedly was suffering from tertiary syphilis. Silver arsphenamin and neo-arsphenamin did little good, and unfortunately there was no opportunity of exhibiting tartar emetic.

GOODMAN,‡ in a very interesting illustrated paper, enters fully into the question of ulcerating granuloma, and describes several cases seen in

*ITURBE, J. and GONZALEZ, E. August, 1922. "Sobre un caso de granuloma venéreo proveniente de la Guayana británica y observado en Venezuela." *Tropical Diseases Bulletin*. Vol. 19. No. 7. P. 602.

†PAROUNAGIAN, M. B. and GOODMAN, H. May, 1922. "Ulcerating granuloma (granuloma inguinale)." *Archives of Dermatology and Syphilology*. Vol. 5. No. 5. P. 597. (Rev. in *Lancet*. 8th July, 1922. P. 83).

‡GOODMAN, HERMAN. 2nd September, 1922. "Ulcerating Granuloma (*Granuloma inguinale*)" *Journal of the American Medical Association*. Vol. 79. No. 10. P. 815.

the tropics and others, including that already mentioned, in New York City.

In all except two, organisms answering to *Calimatobacterium granulomatis* were found. In examining for it one must be careful to avoid surface contamination. It is advisable to employ a local anæsthetic, and to clean and remove a portion of the active margin. This is then trimmed till only deep tissue is left. The latter is washed in saline solution and smears made by expressing the tissue juice.

Attempts at cultivation, animal infection and auto-inoculation failed. The possible association of these Donovan bodies with the Friedländer or *Bacillus mucosus capsulatus* group was tested by cross-agglutination and cross-precipitation work, but with negative results. Their true nature remains unknown, though GOODMAN will not entirely exclude a possible relationship to *Leishmania*. He considers the condition in the light of what is known regarding rhinoscleroma and some other diseases; speaks of its association with syphilis, and describes its cure with antimony.

The discussion on this paper brought out some points of interest, including a reference to another labial case, seen in Texas.

ULCUS TROPICUM.

Another cutaneous lesion, to which considerable attention has recently been directed, is the crippling disorder known under various names but usually called tropical ulcer, or *Ulcus tropicum*.

It is not feasible to pass here in review all the papers recently written regarding it, but, on account of its therapeutic interest, attention may with advantage be directed to an article by SEN* dealing with cases seen in North Palestine. The sores were typical, and contained both spirochætes and fusiform bacilli. Various lines of treatment were tried: antimony, kharsivan, ointments containing different medicaments, boric acid compresses, and formalin, but none proved entirely satisfactory, and recourse was finally had to the following procedure, here given in the author's own words:—

“The ulcer was thoroughly cleaned up with warm normal saline.

A ligature was put on about four inches above the site of the ulcer.

Then the base and the sides were thoroughly touched with pure

*SEN, K. C. August, 1922. “Observations on *Ulcus tropicum* in North Palestine.” *Indian Medical Gazette*, Vol. 57. No. 8. P. 286.

hydrarg. perchlor. tabloid. This was allowed to act for from one-half to one minute, when the ulcer was next thoroughly washed with warm normal saline. This must be as thorough as possible. The ligature was then taken off, and dressing with hypertonic saline three times a day carried on till the ulcer was clean and granulating. Normal saline dressings were then put on till it had almost healed. If there were signs of irritation, which occurred in one case, hot hypertonic saline compresses four times a day relieved the pain, and the inflammation passed off in one day. The only drawback to this treatment is that the touching of the ulcer with pure hydrarg. perchlor., and the period of the action of the same, is painful, but it only lasts for a minute or so."

Apparently treatment by curetting was not employed, but several observers testify to its efficacy.

PELLAGRA.

A note in the *Journal of the Royal Army Medical Corps** for September, 1922, directs attention to the occurrence of cases of pellagra in this country. The returns of the Registrar-General for England and Wales, for the years 1912 to 1921, show 56 deaths certified as being due to pellagra. At Rainhill Asylum, during the years 1913 to 1918, there were 36 indigenous cases, of which 30 proved fatal, while the 109th Report of Royal Edinburgh Asylum has a record of 4 cases during last year, of which 3 ended in death.

Considering that pellagra is now generally regarded as a form of "deficiency disease," possibly with some other etiological factor super-added, it would be interesting to know if the late war occasioned in this country an increase in its incidence.

VOMITING IN MALARIA.

Every practitioner in the tropics knows how troublesome a symptom emesis may be in cases of malaria. Hence a paper by LOMAX WOOD,†

*September, 1922. "Current Literature: Pellagra." *Journal of the Royal Army Medical Corps*. Vol. 39. No. 3. P. 238.

†WOOD, E. LOMAX. December, 1921. "A Note on the Treatment of Vomiting in Malaria." *The Practitioner*. Vol. 107. No. 6. P. 443.

describing a method of treatment for this distressing complication is of special interest. Amongst thirty-eight cases of malaria there were eight of vomiting, and in every one of them it was immediately and effectively controlled by the exhibition of liq. adrenalin hydrochlor. A single dose of from 7 to 8 minims in $1\frac{1}{2}$ to 2 ounces of water sufficed. Not only did the vomiting vanish, but the patients were able to take quinine and nourishment better than had previously been the case. The remedy was given, in the first instance, to check hæmatemesis induced by the straining, but certainly appears to merit further trial in all cases of malaria where vomiting is a prominent symptom.

TROPICAL FISH.

It is not always easy to obtain information about tropical fish used as food, and also as regards fish-poisoning in the tropics. Hence one welcomes an illustrated paper by WALKER,* dealing primarily with fish-poisoning in the Virgin Islands of the United States, but also furnishing particulars about sea fish used for food in the West Indies.

Photographs of a number of these are given, and if anyone interested in the subject will study this paper and then pay a visit to the fish-gallery at the Natural History Museum, South Kensington, he will, in all probability, have added to his knowledge. The fish-gallery now shows, not only marine fish but a number of freshwater species, amongst them the huge and curious *Arapaima gigas*, which is so valuable an article of food in Brazil and the Guianas.

ANDREW BALFOUR.

*WALKER, F. D. August, 1922. "Fish-poisoning in the Virgin Islands." *U.S. Naval Medical Bulletin*. Vol. 17. No. 2. P. 193.

REVIEW.

TSETSE-FLIES.*

AUSTEN's *Monograph of the Tsetse-Flies* appeared in 1903, and his well-known Handbook on the same subject in 1911. Since the latter date a great deal of fresh information regarding the Glossinæ has accumulated, and it was very desirable that this material, scattered through journals and reports, should be collected in one volume. As Lord BUXTON says in his prefatory note, a résumé was published, in 1915, in French by M. EMILE HEGH, of the Belgian Colonial Office, and it was felt by the Honorary Managing Committee of the Imperial Bureau of Entomology that the time had come to produce an English edition of this pamphlet brought up to date in every particular.

Accordingly Major E. E. AUSTEN, D.S.O., has been associated with M. HEGH in the laborious task of compiling this new publication. Needless to say, no better choice could have been made, and a study of the work shows in what a careful and exhaustive manner the authors have searched the literature, whilst their introduction and their comments scattered—perhaps too sparsely—through the text indicate their grasp of a difficult subject, and the well-balanced judgment they bring to bear on many controversial points.

So extensive is the domain through which they lead the enquirer, so rich the scientific pabulum, that the reader, when, with some regret, he comes to the end of this most interesting book, is surprised to find that a great deal still remains to be discovered about tsetse-flies. Yet he is confronted both with a questionnaire and with suggestions for future work, the latter culled from the *Report of the Glossina Sub-Committee of the Imperial Bureau of Entomology*.

**Tsetse-Flies; Their Characteristics, Distribution and Bionomics, with Some Account of Possible Methods for their Control.* By Major E. E. AUSTEN, D.S.O., Assistant-Keeper in the Department of Entomology, British Museum (Natural History), and EMILE HEGH, Chef de Bureau au Ministère des Colonies de Belgique. With Preface by the Earl BUXTON, G.C.M.G., Chairman, Honorary Committee of Management, Imperial Bureau of Entomology. London: The Imperial Bureau of Entomology, 41, Queen's Gate, S.W. 7. 1922. Price, 7s. 6d. nett.

Speaking generally, the book is a work of reference; an admirable review, not so much of the literature as of the findings and the opinions of many field and, to a lesser extent, laboratory workers who have striven to throw light on problems which, in Africa, bulk very largely and are of the greatest economic importance.

It is never easy to review a review. Hence it seems better merely to give some indication of the scope of the work, and to comment briefly on certain points which perhaps possess special interest or importance.

After a short but adequate introduction and a chapter on general characters, geographical distribution and classification, with a mention both of AUSTEN's and NEWSTEAD's grouping, the distinctive characters and geographical distribution of individual species are considered. Then follows a chapter on reproduction, which contains an interesting foot-note on NEWSTEAD's remarkable discovery that the terminal protuberances of the larva act as respiratory organs during its intra-uterine life. The function of the fluid secreted by the larva is discussed, and some doubt is expressed as to the validity of LAMBORN's view that it is of a protective nature. A plate of considerable value is that showing the difference between the pupæ of six species of tsetse. Apparently, under exceptional conditions, parthenogenesis may occur, to judge by the observations of STUHLMAN.

A great deal of information is contained in the chapters dealing with breeding places, the breeding season and "fly-belts."

Here we can only note one significant paragraph, quoted from ROUBAUD's recent work. He says:—

"All causes capable of producing variation in the distribution of big game—hunting forays, epidemics, railway extensions, etc.—will necessarily also have a repercussion on the dispersion of *G. morsitans*, which, in view of this, must be considered much less stable than that of the other tsetse-flies."

Chapter VI. is devoted wholly to a consideration of the distribution of tsetse-flies in Belgian Congo, and many of the facts are likely to be new to British workers.

Points in bionomics form the subject of a chapter dealing with numerous matters which still require elucidation. Here, as elsewhere, due attention is paid to the painstaking observations of SWYNNERTON and of FISKE.

The food of tsetse-flies is fully considered, and amongst the foot-notes, which form not the least interesting part of the volume, there is a reference to the pursuit of fast river steamers by flies on the blood quest.

Perhaps the most important chapters are those concerned with the relation of the flies to the smaller animals and to big game. These should be carefully studied by everyone to whom the subject appeals.

On the subject of game preservation the six questions tabulated by WOOSNAM, as those which must be considered before any plan of campaign can be laid down, are quoted and are as follows :—

“ 1. Are game animals the only wild animals which are acting as ‘ reservoirs ’ for trypanosomes ?

“ 2. Are the trypanosomes found in the blood of game animals pathogenic for man and domestic animals ? And, if so, are not the trypanosomes found in the blood of other animals also pathogenic ?

“ 3. Are tsetse-flies the only transmitting agents of these trypanosomes in the infected areas ?

“ 4. Are game animals the only source from which the tsetse-flies or other transmitting agents draw their blood supply ? And, if not, what are the other sources of supply ?

“ 5. Can tsetse-flies live and breed upon food other than blood, such as plant juices ?

“ 6. Are the distribution, increase and spread of tsetse-flies, if this latter occurs, dependent upon game alone ? And, if not, what are the governing factors ? ”

Of course, several of these have been answered more or less completely.

The effect of external factors is briefly noted, together with MACFIE'S experiments, and then the whole question of prevention is discussed in all its bearings. The enemies and parasites of the flies are described and illustrated. Clearing, trapping, the use of repellents, personal protection of human beings, and the destruction of big game receive attention, and are the subject of that judicious comment which is such a feature of the book.

Lastly, there are chapters to aid the collector, the entomologist, and the laboratory worker, and the volume concludes with the questionnaire and the suggestions already mentioned.

There is a useful list of references, some excellent illustrations, and an adequate index.

This volume cannot fail to be of the greatest service to all students of tropical medicine, and is indispensable to those who are concerned with investigations regarding human sleeping sickness and animal trypanosomiasis in Africa. The only adverse criticism that can be advanced is that the paper cover is quite inadequate. It is a pity that a work to which constant reference must be made was not more suitably bound.

ANDREW BALFOUR.

POSTSCRIPT TO DR. J. W. S. MACFIE'S PAPER

On "Prevalent Diseases of the Gold Coast," which appeared in the last number of the TRANSACTIONS (No. 3).

Dr. MACFIE writes:—

"I have recently (August, 1922) diagnosed a case of diphtheria at Accra in a native boy aged four years. The bacillus isolated from the throat corresponded with *B. diphtheriæ* in morphological and cultural characters, produced acid from glucose and dextrin, but not from saccharose in Hiss serum-water media, and was acutely pathogenic to guinea-pigs. The case, which proved fatal, was clinically somewhat atypical.

FAR EASTERN ASSOCIATION OF TROPICAL MEDICINE.

At the fourth Congress of the Far Eastern Association of Tropical Medicine, which was held at Weltevreden, Java, in August, 1921, a proposal was made on behalf of the Governments of the Straits Settlements and Federated Malay States by their delegate, Dr. A. E. HORN, that the next Congress of the Association be held in Malaya.

The laws of the Association provide that the meetings shall be held every two years, and as the proposal was accepted, the Congress will meet in Malaya in 1923.

Dr. A. E. HORN was chosen President for the forthcoming session.

Drs. A. L. HOOPS and R. DOWDEN were elected as Vice-Presidents for the Straits Settlements and Federated Malay States, and Dr. J. W. SCHARFF as Honorary Secretary for Malaya.

On the 21st April, 1922, a meeting was held to elect Committees for the organisation of the Congress. Subsequently other meetings were held, and definite schemes were prepared for the management of Congress. It has been decided to hold the meeting from September 3rd to 17th. The first week of this period will be devoted to scientific discussions, and the following week to excursions to points of medical and sanitary interest throughout Malaya.

The Governments of the Straits Settlements and Federated Malay States have recognised the important functions of this Association, and are contributing a considerable sum towards the expenses.

The object of this Association is to promote the science and art of tropical medicine in the Far East. For this purpose the Association endeavours to unite into one compact organisation the medical profession of the Far East for the growth and diffusion of medical knowledge; to promote friendly international intercourse among physicians; to elevate the standard of medical education; to enlighten and direct public opinion in regard to the problems of hygiene; to form habits which may conduce

to the prevention of disease among the native population ; and to present to the world the results of such scientific observations.

The membership of this Association consists of the members of all duly constituted, regularly organised medical societies within the field of this organisation, and all medical officials in the civil, military, naval, or other organised services of Governments within their territories.

It is requested that those who wish to submit papers will communicate with the Honorary Secretary as soon as possible.

NEW FELLOWS.

The following were duly elected Fellows of the Society on 19th Oct., 1922 :—

- G. J. P. BARGER, M.D. (Harvard), Congo Belge.
WILLIAM CORNER, O.B.E., M.B., Ch.B., Baghdad.
EDWIN CHARLES CORT, M.A., M.D., Siam.
VERNON DAVIES, D.S.O., M.D. (Melb.), Vila. New Hebrides.
WILLIAM DUNLOP, O.B.E., M.B., Ch.B. (Edin.), Baghdad.
JOHN REID FORDE, M.B., Ch.B., B.A.O., Gold Coast.
WILLIAM ARTHUR FRYMIRE, M.D., Congo Belge,
F. MURRAY HALLEY, M.B., Ch.B. (Edin.), Baghdad.
T. BARRETT HEGGS, M.D. (Aber.), D.P.H. (Cantab.), M.O.H., Baghdad.
FRANK S. HOWE, B.A., M.B., B.S., South Australia.
R. B. LAL, M.B., B.S. (Punjab), D.T.M. & H. (Eng.), D.P.P. (Oxon.),
India.
JAMES W. MCKEAN, M.A., M.D., Siam.
Lieut.-Col. F. P. MACKIE, O.B.E., M.D., M.Sc., F.R.C.S., L.R.C.P., I.M.S.,
Assam.
L. M. MOODY, M.D., B.S., M.R.C.P., D.T.M. & H., Jamaica.
Prince MOM CHOW THAVARA, M.R.C.S. (Eng.), L.R.C.P. (Lond.), Siam.
FORBES WILLIAM SANDISON, O.B.E., M.C., M.B., Ch.B., Baghdad.
NORBERT SEPPELT, L.R.C.P. & S.E., Burma.
Major PATRICK MANSON RENNIE, M.B., Ch.B., D.P.H. (Aber.), D.T.M. & H.
(Cantab.), I.M.S.
MICHAEL S. VASSALLO, M.D., D.T.M. & H., Uganda.
ARTHUR T. WILLIAMS, B.A. (Oxon.), M.R.C.S. (Eng.), L.R.C.P. (Lond.),
Assam.
-

FELLOWS DECEASED.

- Dr. CLEMENT J. BAKER, of Uganda.
Dr. LEOPOLD G. HILL, of London.
Professor STEPHEN KARTULIS, of Egypt.
Dr. ALAN KIDD, of Ceylon.
Dr. A. YALE MASSEY, of the Belgian Congo.

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MOVEMENTS OF FELLOWS.

The following Fellows have notified the Secretaries that they are at present in England :—

- J. COTTER BAKER, M.B., India.
 D. BASU, M.B., India.
 A. BINDARY, Egypt.
 RUPERT BRIERCLIFFE, O.B.E., Palestine.
 W. J. BRUCE, M.R.C.S., Gold Coast.
 G. G. BUTLER, M.B., Tanganyika.
 P. A. BUXTON, M.R.C.S., L.R.C.P., Palestine.
 DONALD W. CARR, M.D., Persia.
 C. C. CHESTERMAN, O.B.E., Belgian Congo.
 N. CRITCHLOW, M.B., Ch.B., British Solomon Islands.
 J. DALRYMPLE, C.M.G., O.B.E., South Africa.
 R. DOWDEN, M.D., D.T.M., Kuala Lumpur.
 J. DUNLOP, M.B., India.
 J. J. B. EDMOND, M.B., Ch.B., Tanganyika.
 Col. G. WYKEHAM HERON, D.S.O., O.B.E., M.R.C.S., L.R.C.P., Palestine.
 Major R. KELSALL, D.S.O., M.D., Burmah.
 V. T. KORKE, M.R.C.P., India.
 Lieut.-Col. W. GLEN LISTON, C.I.E., India.
 J. W. S. MACFIE, M.B., Gold Coast.
 LUCIUS NICHOLLS, M.D., Ceylon.
 Major W. H. PEACOCK, M.B., M.R.C.S., Sierra Leone.
 E. J. QUIRK, M.B.E., Nigeria.
 A. A. RASIK, M.R.C.S., L.R.C.P., Egypt.
 C. B. B. REID, M.B., Kenya Colony.
 Capt. BASIL H. H. SPENCE, M.B., R.A.M.C., Sudan.
 Major W. D. H. STEVENSON, C.I.E., M.A., M.D., D.P.H., India.
 VAN SOMERAN TAYLOR, M.B., China.
 ANDREW TOPPING, M.A., M.B., Persian Gulf.
 Lieut.-Col. J. N. WALKER, I.M.S., India.
 A. R. WELLINGTON, M.R.C.S., D.P.H., Federated Malay States.
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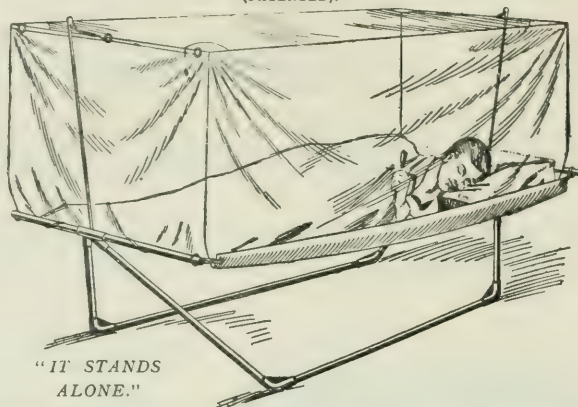
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REPRINT OF COLONEL A. ALCOCK'S ARTICLE ON SIR PATRICK MANSON.

Attention is drawn to the illustrated article on the late Sir PATRICK MANSON by Colonel A. ALCOCK, F.R.S., which appeared in the TRANSACTIONS, Vol. XVI., No. 2.

Fellows, and others interested, should note that they can obtain *Reprints of the Illustrated Article* for 2s. 6d., or the *Set of Three Portraits* for 1s. 6d. Application for these, enclosing remittance, should be addressed to the Secretaries, 11, Chandos Street, Cavendish Square, London, W. 1.

EDITORIAL NOTICES.

The Editor of the TRANSACTIONS will be pleased to receive short papers to be included under the heading of "Communications" or "Questions," in addition to longer papers on subjects of Tropical interest, which may be offered for presentation at meetings of the Society. He will also be glad to receive books for review.

Attention is drawn to the rule that Contributors of papers to the TRANSACTIONS receive 25 reprints free of charge, *provided they apply for these when sending the paper.*

Any communication for the Editor should be addressed to THE EDITOR of the TRANSACTIONS of the Royal Society of Tropical Medicine and Hygiene 11, Chandos Street, Cavendish Square, W. 1.

Complete sets of the first four volumes of the TRANSACTIONS belonging to the Society have now become very scarce. If any Fellows possess these volumes, or any odd numbers of the same, and no longer require them, the Council would be greatly obliged if they could be presented to the Society.

There are frequent applications for these volumes from Libraries which are desirous of completing their sets. At the present time it is impossible to meet these requests, and it is felt that it would be doing a service to the cause of science to help them as far as possible.

CHALMERS AND MANSON MEDALS.

The attention of Fellows is directed to the notice of the conditions of award of the CHALMERS and MANSON Medals in the new Year Book of the Society, the first awards of which are to be made in 1923. They will note that the nominations for the MANSON Medal are to be made by the Council only, whereas any Fellow of the Society is entitled to nominate for the CHALMERS Medal. Fellows who wish to make a nomination for the CHALMERS Medal are requested to submit to the Hon. Secretaries, not later than 28th February, 1923, the name of their nominee, together with a written statement as to his claims according to the conditions of award published in the Year Book, which must be fully complied with.

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PUBLISHING NOTICES.

NOTICE TO FELLOWS.

A copy of the TRANSACTIONS will be posted regularly to every Fellow. It was decided by the Council to discontinue issuing TRANSACTIONS to Fellows who had not paid their subscription by June in the year following that in which it was due. The subscription falls due on 1st of April of each year.

Fellows are requested to give early intimation of any change of address, and in case of non-delivery of their copies of the TRANSACTIONS to communicate with the Secretaries as soon as possible. When copies of the TRANSACTIONS are returned by the Post Office, marked "gone away" or "insufficiently directed," no more copies will be posted to that address until further instructions have been received.

SPECIAL NOTE.—Complaints are sometimes received of the TRANSACTIONS not reaching Fellows abroad. In almost every instance, when the matter has been looked into, it has been found that the Fellow has changed his original address and has not notified this change to the Secretaries at home.

Unless this is done, it is impossible for the TRANSACTIONS to be regularly received, and the Secretaries hope that Fellows will be more careful about this in future.

All communications should be addressed to—

THE SECRETARIES,

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE,

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Copies of the TRANSACTIONS may be obtained by Non-Fellows from Messrs. J. C. PHELP & SON, Beulah Road, Walthamstow, E. 17. There are six issues each session, two being double numbers. The price is 5s. net single numbers and 7s. 6d. net double numbers, or 35s. per ann., postage extra.

Fellows of the Society are reminded that they can only obtain their copies through the Secretaries.

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